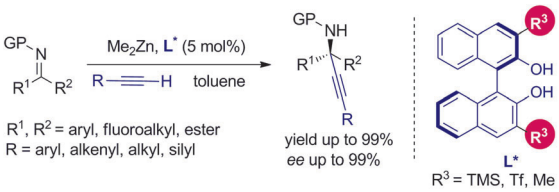

Propped up: A Zn/BINOL-catalyzed method for the enantioselective alkynylation of ketoimines, including α-fluoroalkyl α-imine esters, α-aryl α-imine esters, and trifluoromethyl aryl ketoimines, is described (see scheme; PG = protecting group, TMS = trimethylsilyl, Tf = triflyl). The corresponding quaternary propargyl amines are produced in excellent yields with high *ee* values (up to 99% *ee*).

Enantioselectivity

*G. Huang, Z. Yin, X. Zhang**..... ■■■■–■■■■

Construction of Optically Active Quaternary Propargyl Amines by Highly Enantioselective Zinc/BINOL-Catalyzed Alkynylation of Ketoimines

Chinese mythology...... was used to describe the challenges involved in the catalytic enantioselective alkynylation of ketoimines. The arrow shows the alkynylzinc reagent generated from alkyne and Me_2Zn; BINOL, an accelerator for the reaction, is the bow. The substrates ketoimines are the suns. The three suns shot down in the sea are the three types of products, chiral quaternary propargyl amines. For more details, see the Full Paper by X. Zhang et al. on page ■■ff.

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Construction of Optically Active Quaternary Propargyl Amines by Highly Enantioselective Zinc/BINOL-Catalyzed Alkynylation of Ketoimines

Gaochao Huang, Zengsheng Yin, and Xingang Zhang*[a]

Abstract: A general and efficient method for the highly enantioselective alkynylation of ketoimines through a zinc/1,1′-bi-2-naphthol (BINOL)-catalyzed process has been developed. A variety of ketoimines, including α-fluoroalkyl α-imine esters, α-aryl α-imine esters, and trifluoromethyl aryl ketoimines, are applicable and provide their corresponding quaternary propargyl amines in excellent yields with high *ee* values (up to 99% *ee*). Both the steric and electronic effects of substituents at the 3,3′ positions of BINOL are critical for the reaction efficiency and enantioselectivity. To demonstrate the usefulness of the method, (*R*)-α-CF_3 α-proline has been prepared in a highly efficient manner. The notable features of this protocol are its broad substrate scope, high reaction efficiency (up to 99%) and enantioselectivity (up to 99% *ee*), low catalyst loading (5 mol% of BINOL derivative), and mild reaction conditions.

Keywords: alkynylation · amino acids · BINOL · ketoimines · propargyl amines · zinc

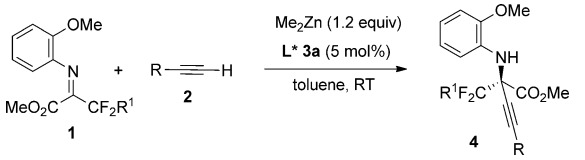
Introduction

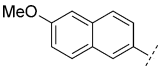
Developing new methods to prepare optically active propargyl amines, including quaternary propargyl amino acids and related derivatives, is of great importance due to the synthetic utility of chiral propargyl amines in the total synthesis of natural products and pharmaceutical compounds.[1] The most widely used approaches to these important synthetic building blocks rely on the asymmetric alkynylation of imines.[2] Over the past several years, great endeavors have been devoted to this area and some impressive protocols with high enantioselectivities and yields resulting from the addition of terminal alkynes to aldimines have been reported.[3,4] To date, however, the catalytic enantioselective alkynylation of ketoimines is still a challenge because of the low reactivity and difficulties in enantiofacial discrimination of ketoimines.[5,6] Thus, new methods that meet these challenges for widespread synthetic application are highly desirable.[7]

Meanwhile, enantiomerically enriched quaternary α-amino acids or related derivatives are found in many biologically active compounds[8] and lend conformational rigidity to biologically active peptides.[9] In particular, the incorporation of α-fluorinated amino acids into peptides leads to great changes in their biological activity by improving enzymatic stability and enhancing in vivo absorption and drug permeability through certain body barriers.[10] Hence, it is of great interest to prepare these valuable building blocks.

Very recently, we reported a first example of the catalytic enantioselective alkynylation of ketoimine (α-CF_3 ketoimine ester) by a zinc/1,1′-bi-2-naphthol[11] (BINOL)-catalyzed process (Table 1, entries 1 and 2).[7a] As part of our continued efforts in this area,[12] we herein describe a general method for the catalytic enantioselective alkynylation of acyclic ketoimines by a zinc/BINOL-catalyzed process (Scheme 1). The advantages of this protocol are a broad

Table 1. Catalytic enantioselective addition of terminal alkynes **2** to α-ketoimine esters **1**.[a]



Entry	**1**	R^1	**2**	R	**4** Yield [%][b]	*ee* [%][c]
1	**1a**	F	**2a**	Ph	**4a**, 90	97
2	**1a**	F	**2b**		**4b**, 91	98
3	**1b**	Br	**2a**	Ph	**4c**, 94	94
4	**1b**	Br	**2c**		**4d**, 91	89
5	**1b**	Br	**2b**		**4e**, 86	96
6[d]	**1b**	Br	**2d**	$BnOCH_2$	**4f**, 88	92
7	**1c**	Cl	**2a**	Ph	**4g**, 83	96
8	**1d**	CF_3	**2a**	Ph	**4h**, 95	95
9	**1d**	CF_3	**2b**		**4i**, 76	96
10	**1e**	allyl	**2a**	Ph	**4j**, 92	95

[a] Reaction conditions unless otherwise specified: **1** (0.3 mmol), **2** (1.7 equiv), Me_2Zn (1.2 equiv), **L*3a** (5 mol%), toluene (1.2 mL), 19–48 h, RT. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] With 2.5 equiv of **2**.

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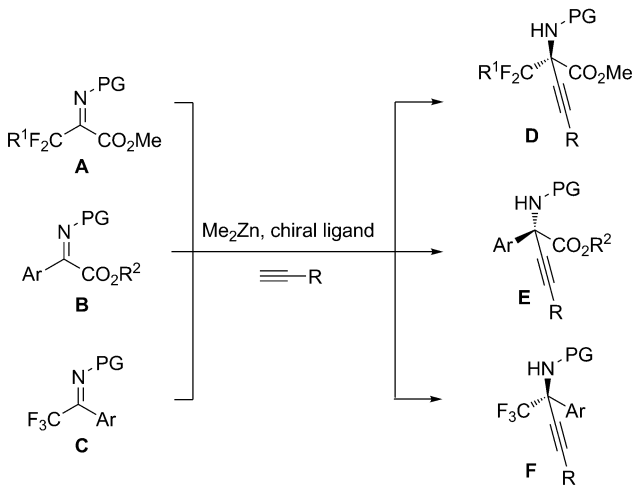


Scheme 1. Zinc/BINOL-catalyzed alkynylation of acyclic ketoimines; PG = protecting group.

substrate scope for both terminal alkynes and acyclic ketoimines, a high reaction efficiency and enantioselectivity (up to 99% *ee*), low catalyst loading (5 mol% of BINOL derivative), and mild reaction conditions (room temperature). This protocol provides an efficient method for the preparation of optically active quaternary α-amino acids, including α-fluoroalkyl amino acids.

Results and Discussion

Enantioselective alkynylation of α-fluoroalkyl α-imine esters: Fluorinated amino acids are important building blocks in the field of peptide design and protein engineering due to the unique properties of fluorine atom(s). However, limited methods for the enantioselective synthesis of fluorinated amino acids have been developed so far.[13] In particular, few examples of the catalytic enantioselective synthesis of α-fluoroalkyl α-amino acids have been reported.[14] Inspired by our recent work, a variety of fluorinated α-ketoimine esters **1**, including functionalized difluoromethyl and perfluoroalkyl α-ketoimine esters,[15] were investigated. As illustrated in Table 1, different optically active α-fluoroalkyl α-amino acids were obtained by reaction of **1** (1.0 equiv) with alkynes **2** (1.7 equiv) and Me_2Zn (1.2 equiv) in the presence of (*R*)-3,3′-TMS_2-BINOL (**3a**, TMS = trimethylsilyl; 5 mol%) in toluene at room temperature. Generally, the nature of the substituent R^1 did not influence the reaction efficiency and enantioselectivity. Ketoimines **1b–c**, containing bromo- and chloro- difluoromethyl groups, were tolerated in the reaction systems with Br and Cl atoms remaining intact, and gave alkynylated products **4c–g** in good yields with excellent *ee* values of up to 96% (Table 1, entries 3–7). This allowed for the further formation of carbon–carbon bonds or carbon–heteroatom bonds by transition-metal-mediated coupling and other reactions (i.e., radical reactions). High *ee* values (95–97%) and good yields were also obtained when perfluoroalkylated substrate **1d** was tested (Table 1, entries 8 and 9). The functionalized allyl-substituted α-ketoimine ester **1e** also underwent the reaction smoothly to provide a good yield and high *ee* value (Table 1, entry 10). It should be pointed out that these resulting difluorinated propargyl amines can also serve as a class of important building blocks for the synthesis of biologically active compounds; the incorporation of a geminal difluoromethlene group (CF_2) into an organic molecule can not only enhance the acidity of its neighboring groups, but also act as an isopolar–isosteric substitute for oxygen.[16] The configuration of **4** was determined to be *R* by X-ray crystal structure analysis of **4d** (Figure 1).[17]

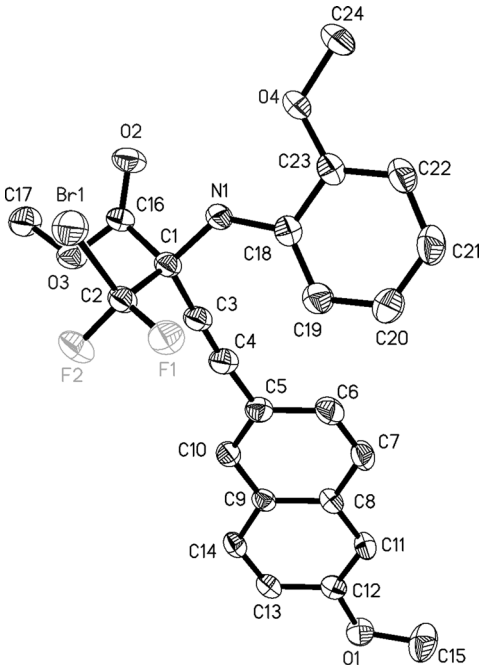
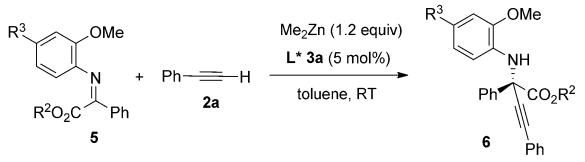


Figure 1. X-ray crystal structure of compound **4d**. Hydrogen atoms have been removed for clarity, ellipsoids are shown at the 30% probability level.

Catalytic enantioselective alkynylation of α-aryl α-imine esters:[17,18] To further probe the applicability of this method, we turned our attention to the relatively less reactive α-aryl α-imine esters. A dramatically decreased yield and enantioselectivity were observed when the α-phenyl α-imine ester **5a** was subjected to the same reaction conditions (Table 2, entry 1). To address the issue, an electron-withdrawing group NO_2 was introduced into the N-protecting group to enhance the electrophilicity of **5a**. As expected, the yield was significantly increased, although no enantioselectivity was observed (Table 2, entry 2). Considering that the steric effect of both substituents in ketoimine plays a critical role in the enantioselectivity of the reaction, and that different sizes of these two substituents benefit the enantiofacial discrimination of ketomine, we then tuned the size of the ester group to improve the reaction enantioselectivity (Table 2,

Table 2. Optimization of catalytic enantioselective addition of terminal alkyne **2a** to α-aryl α-imine esters **5**.[a]



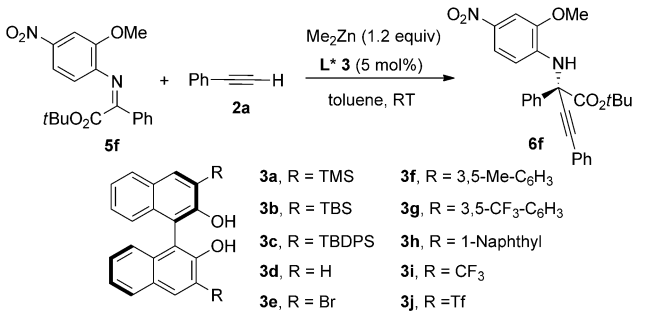
Entry	Imine **5**	R^2	R^3	Yield [%][b]	*ee* [%][c]
1	**5a**	Me	H	**6a**, 19	19
2	**5b**	Me	NO_2	**6b**, 82	0
3	**5c**	Cy	NO_2	**6c**, 90	34
4	**5d**	*i*Pr	NO_2	**6d**, 78	43
5	**5e**	1-Ad	NO_2	**6e**, 96	72
6	**5f**	*t*Bu	NO_2	**6f**, 82	77

[a] Reaction conditions unless otherwise specified: **5** (0.3 mmol), **2a** (1.7 equiv), Me_2Zn (1.2 equiv), **3a** (5 mol%), toluene (1.2 mL), 19–48 h, RT. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis.

entries 3–6). It turned out that a *tert*-butyl group was the best choice, providing a good yield (82%) and moderate *ee* (77%; Table 2, entry 6). Changing the *tert*-butyl group to a cyclohexyl (Cy) or 1-adamantyl (1-Ad) group led to higher yields but lower enantioselectivities (Table 2, entries 3 and 5).

After identification of the suitable α-phenyl α-imine ester substrate **5f**, different BINOL-type ligands **L*3**, modified at the 3,3′ positions, were evaluated in an effort to further improve the enantioselectivity (Table 3). We found that the

Table 3. Screening of chiral ligands for the catalytic enantioselective addition of terminal alkyne **2a** to α-phenyl α-imine ester **5f**.[a]



Entry	**L*3**	Yield [%][b]	*ee* [%][c]
1	**3a**	82	77
2	**3b**	93	19
3	**3c**	93	88
4	**3d**	99	60
5	**3e**	99	74
6	**3f**	80	19
7	**3g**	99	96
8	**3h**	75	55
9	**3i**	99	81
10	**3j**	98	98

[a] Reaction conditions unless otherwise specified: **5f** (0.3 mmol), **2a** (1.7 equiv), Me_2Zn (1.2 equiv), **L*3** (5 mol%), toluene (1.2 mL), 19–48 h, RT. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis.

electronic effects of the substituents at positions 3,3′ of BINOL are critical to the enantioselectivity. For instance, the CF_3-containing ligand **3g** provided a much higher *ee* value than its nonfluorinated counterpart **3f** (Table 3, entries 6 and 7), suggesting that an electron-withdrawing group benefits the enantioselectivity. But bulky substituents were less effective, low *ee* values were observed (Table 3, entries 2, 3 and 8). With these findings in mind, CF_3- and Tf-substituted ligands **3i** and **3j** were further evaluated (Table 3, entries 9 and 10). To our delight, an excellent *ee* (98%) and yield (98%) were obtained when **3j** was used (Table 3, entry 10).

With the optimized reaction conditions established (Table 3, entry 10), the substrate scope of the catalytic enantioselective alkynylation of α-aryl α-imine esters **5** with alkynes **2** was investigated (Table 4). Generally, imine esters **5** containing different aryl groups underwent the reaction smoothly with excellent yields (92–98%) and high *ee* values (86–98%; Table 4, entries 1–6). Notably, the bromide-containing substrate **5j** successfully furnished the corresponding propargyl amine in excellent yield with high enantioselectivity (97% *ee*; Table 4, entry 5). Naphthyl groups were also tolerated in the catalytic system (Table 4, entry 6). A variety of terminal alkynes, including aryl-, alkyl-, and silyl-substituted alkynes, were also examined (Table 4, entries 7–13). For aromatic and conjugated terminal alkynes, excellent yields and high *ee* values were obtained (Table 4, entries 7–10). In particular, aliphatic and silyl-substituted terminal alkynes gave high *ee* values, providing opportunities for further transformations (Table 4, entries 11–13). The configuration of **6** was determined to be *S* by X-ray crystal structure analysis of **6j** (Figure 2).[17]

Catalytic enantioselective alkynylation of trifluoromethyl aryl ketoimines:[17,19] Chiral fluorinated amines have re-

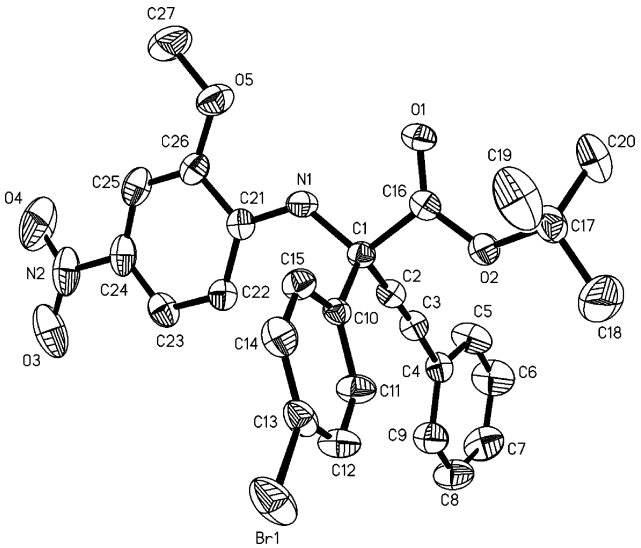
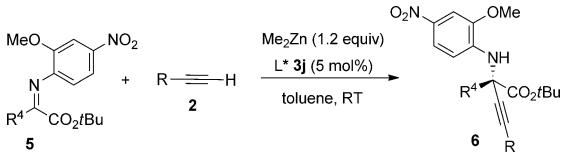


Figure 2. X-ray crystal structure of compound **6j**. Hydrogen atoms have been removed for clarity, ellipsoids are shown at the 30% probability level.

Table 4. Catalytic enantioselective addition of terminal alkynes **2** to α-phenyl α-imine esters **5**.[a]



Entry	Imine **5**	R^4	Alkyne **2**	R	**6**, Yield [%][b]	*ee* [%][c]
1	**5f**	Ph	**2a**	Ph	**6f**, 98	98
2	**5g**	MeO	**2a**	Ph	**6g**, 92	89
3	**5h**	F_3C	**2a**	Ph	**6h**, 95	86
4	**5i**	Me	**2a**	Ph	**6i**, 98	99
5	**5j**	Br	**2a**	Ph	**6j**, 96	97
6	**5k**		**2a**	Ph	**6k**, 98	96
7	**5f**	Ph	**2e**	Cl	**6l**, 97	99
8	**5f**	Ph	**2f**	MeO	**6m**, 96	91
9	**5f**	Ph	**2g**	EtO_2C	**6n**, 97	93
10[d]	**5f**	Ph	**2h**		**6o**, 98	98
11	**5f**	Ph	**2b**		**6p**, 97	89
12[d]	**5f**	Ph	**2i**	n-C_7H_{15}	**6q**, 92	87
13[e]	**5f**	Ph	**2j**	TMS	**6r**, 84	91

[a] Reaction conditions unless otherwise specified: **5** (0.3 mmol), **2** (1.7 equiv), Me_2Zn (1.2 equiv), **3j** (5 mol%), toluene (1.2 mL), 19–48 h, RT. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] With 2.5 equiv of **2**. [e] With 5.0 equiv of **2**.

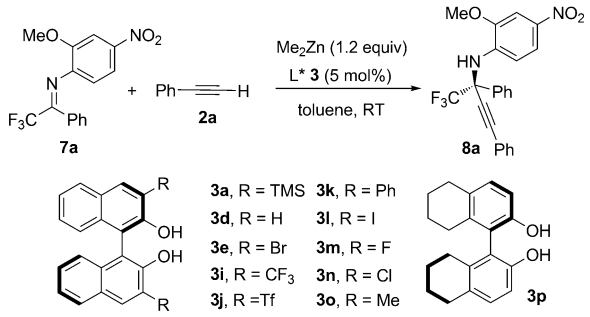
ceived considerable interest due to their importance in pharmaceuticals and materials science.[14a] Although many synthetic methods to produce these valuable fluorinated compounds have been developed, few catalytic enantioselective approaches have been reported.[20] To further extend the substrate scope of this method, the zinc/BINOL-catalyzed alkynylation of trifluoromethyl aryl ketoimines was investigated (Table 5). Unexpectedly, none of the desired product **8a** was observed when ketoimine **7a** was treated with alkyne **2a** under the standard reaction conditions identified previously for the synthesis of compounds **4** (Table 5, entry 1). We surmised that the negative result may arise from the use of the bulky ligand (*R*)-3,3′-$(TMS)_2$-BINOL (**3a**), which blocks the attack of the alkynyl-Zn/BINOL complex to the ketoimine **7a**. Accordingly, the TMS groups at the 3,3′ positions of BINOL were changed to smaller phenyl groups. To our delight, a 62% yield of **8a** was obtained, albeit in low enantiomeric excess (Table 5, entry 2). Further investigation of the ligand **3** with a much smaller methyl group resulted in a dramatically improved enantioselectivity and reaction efficiency. Encouraged by these results, a series of BINOL-type ligands **3** with small substituents at the 3,3′ positions were examined (Table 5, entries 3–10). We found that even when the BINOL **3d** was used, a good enantioselectivity could still be obtained (Table 5, entry 10). In contrast, a low enantiomeric excess was observed when (*R*)-3,3′-F_2-BINOL was examined, suggesting that the electronic effect of the substituents at the 3,3′ positions of BINOL is also critical to the reaction enantioselectivity (Table 5, entry 9). Interestingly, when the BINOL-type ligands with electron-deficient substituents CF_3 or Tf were explored, an enantiomer with the opposite configuration was obtained as the major product (Table 5, entries 4 and 5). A similar finding was also observed when (*R*)-8*H*-BINOL (**3p**) was investigated (Table 5, entry 11), demonstrating that we can obtain both enantiomers enantioselectively by choosing a suitable ligand.

To further optimize the reaction conditions, the reaction temperature was examined (Table 6). It was found that the enantioselectivity was sensitive to the reaction temperature; different temperatures led to different enantioselectivities. To our delight, the highest *ee* value (94%) was obtained when the reaction was performed at 30°C (Table 6, entry 4). However, higher or lower reaction temperatures resulted in lower *ee* values (Table 6, entries 1–3, 5, and 6). Unexpectedly, when the reaction temperature was cooled to 0–5°C, an opposite enantiomeric excess was obtained (Table 6, entry 1). Thus, both enantiomers of **8** can be selectively synthesized by tuning the reaction temperature.

With the optimal reaction conditions in hand, the scope of the catalytic enantioselective addition of terminal alkynes **2** to trifluoromethyl aryl ketoimines **7** was explored. As shown in Table 7, ketoimines **7** possessing different aryl groups gave chiral propargyl amines **8** in excellent yields with good enantioselectivities (Table 7, entries 2–5). In the case of *para*-trifluoromethylphenyl-substituted **7c**, only a modest *ee* value was achieved (Table 7, entry 3). Thiophenyl-substituted **7f** also furnished the corresponding product **8f** in excellent yield and good enantioselectivity (Table 7, entry 6). Importantly, vinyl trifluoromethyl ketoimine **7h** underwent the reaction smoothly without 1,4-addition byproducts being observed (Table 7, entry 8). A variety of terminal alkynes, including those with aryl- and alkyl-substituents, are all suitable substrates, providing their corresponding chiral propargyl amines **8** in excellent yields and enantioselectivities (Table 7, entries 9–15). The configuration of **8** was determined to be *S* by X-ray crystal structure analysis of **9**, which was synthesized from **8o** (Scheme 2a).[17] Further transformation of compound **9** with a Sonogashia reaction gave compound **10** in good yield, thus providing an efficient way to access diverse optically active fluorinated quaternary propargyl amines.

The protecting group on the nitrogen of propargyl amines can be easily removed. As shown in Scheme 2b, hydrogenation of **8a** provided compound **11** in quantitative yield. The resulting amine **11** was then treated with cerium (IV) diam-

Table 5. Screening chiral ligands for catalytic enantioselective addition of terminal alkyne **2a** to trifluoromethyl aryl ketoimine **7a**.[a]



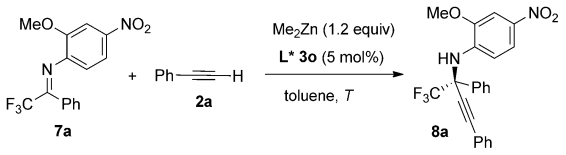
Entry	L*3	Yield [%][b]	*ee* [%][c]
1	**3a**	NR	–
2	**3k**	62	27
3	**3o**	100	88
4	**3i**	100	−43
5	**3j**	21	−72
6	**3e**	57	77
7	**3l**	99	71
8	**3n**	90	60
9	**3m**	100	25
10	**3d**	83	86
11	**3p**	97	−83

[a] Reaction conditions unless otherwise specified: **7a** (0.3 mmol), **2a** (1.7 equiv), Me_2Zn (1.2 equiv), **L*3** (5 mol%), toluene (1.2 mL), 19–48 h, RT. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis.

monium nitrate (CAN) in the presence of H_2SO_4 to give optically acitve quaternary amine **12** in 80% yield.

Transformation of chiral quaternary propargyl amines to optically active α-fluoroalkyl α-amino acids: To demonstrate the usefulness of this method, the transformation of chiral quaternary propargyl amines to the optically active α-fluoroalkyl α-amino acid was performed. As illustrated in Scheme 3, (*R*)-α-CF_3 α-proline (**15**), an important building block in the conformation of peptides and proteins, can be easily obtained in four steps with high efficiency from the chiral propargyl amine **4k**. To the best of our knowledge, this is the first example of the enantioselectively catalyzed synthesis of **15** so far.[21]

Table 6. Investigation of reaction temperature of enantioselective addition of terminal alkynes **2a** to trifluoromethyl aryl ketoimine **7a**.[a]

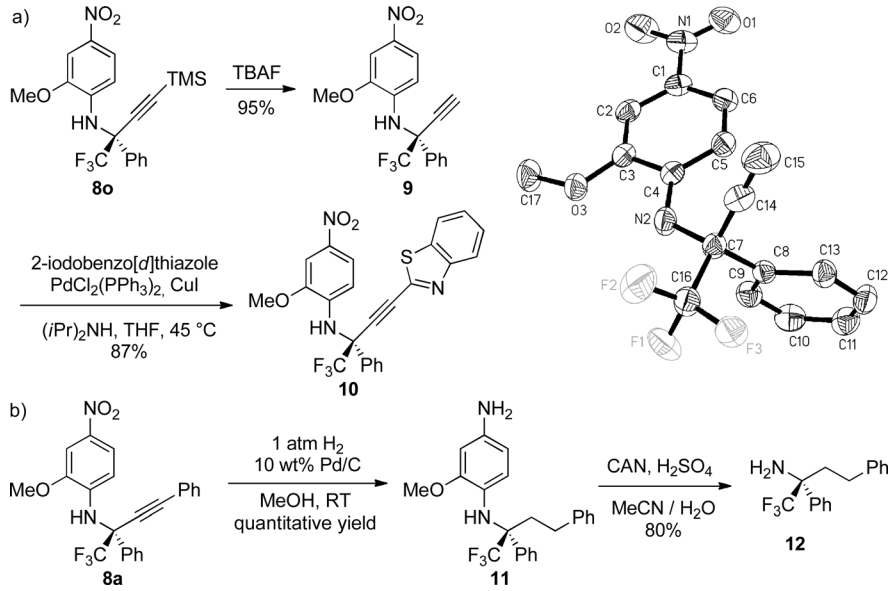


Entry	*T* [°C]	Yield [%][b]	*ee* [%][c]
1	0–5	100	−44
2	17–25	100	59
3	25	100	88
4	30	98	94
5	35	98	87
6	40	97	87

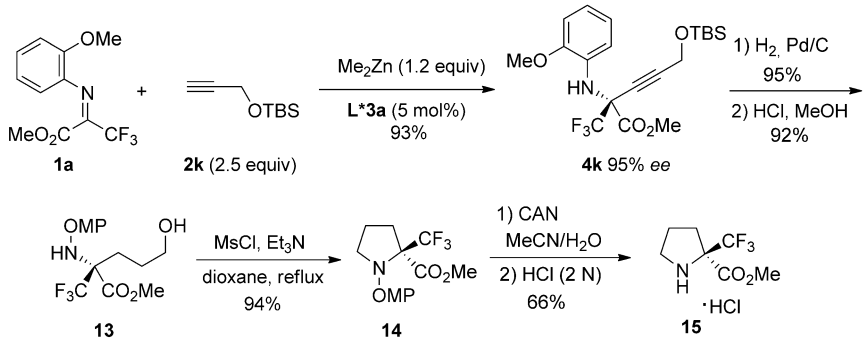
[a] Reaction conditions unless otherwise specified: **7a** (0.3 mmol), **2a** (1.7 equiv), Me_2Zn (1.2 equiv), **L*3o** (5 mol%), toluene (1.2 mL), 19–48 h. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis.

Conclusion

A general and efficient method for the enantioselective alkynylation of ketoimines has been developed by using a zinc/BINOL-catalyzed process. Both the electronic and steric effects of substituents at the 3,3′ positions of BINOL-type ligand are critical for the reaction enantioselectivity. Notably, both enantiomers of the quaternary propargyl amines can be enantioselectively obtained by tuning the electronic properties of the BINOL-type ligand or the reaction temperature, providing a convenient way to access these important building blocks. This method led to the synthesis of the important α-fluoroalkyl α-amino acid in a highly efficient manner, thus demonstrating the usefulness of the protocol. Because of its broad substrate scope, high reaction efficiency and enantioselectivity, low catalyst loading (5 mol% BINOL derivative),

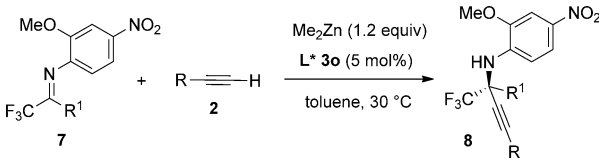


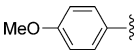
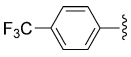
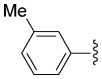
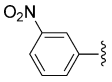
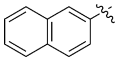
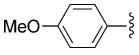
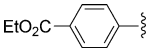
Scheme 2. Determination of the absolute configuration of **8o** by X-ray crystal structure analysis of compound **9** and synthesis of compounds **10** and **12**.



Scheme 3. Synthesis of compound **12** and (*R*)-α-trifluoromethyl proline (**15**).

Table 7. Catalytic enantioselective addition of terminal alkynes **2** to trifluoromethyl aryl ketoimines **7**.[a]



Entry	Imine **7**	R^1	Alkyne **2**	R	**8**, Yield [%][b]	*ee* [%][c]
1	**7a**	Ph	**2a**	Ph	**8a**, 98	94
2	**7b**		**2a**	Ph	**8b**, 92	90
3	**7c**		**2a**	Ph	**8c**, 96	55
4	**7d**		**2a**	Ph	**8d**, 98	91
5	**7e**		**2a**	Ph	**8e**, 98	86
6	**7f**		**2a**	Ph	**8f**, 95	84
7	**7g**		**2a**	Ph	**8g**, 95	92
8	**7h**		**2a**	Ph	**8h**, 97	86
9	**7a**	Ph	**2e**		**8i**, 96	85
10	**7a**	Ph	**2f**		**8j**, 94	85
11	**7a**	Ph	**2g**		**8k**, 98	89
12[d]	**7a**	Ph	**2h**		**8l**, 95	93
13[d]	**7a**	Ph	**2i**		**8m**, 91	88
14	**7a**	Ph	**2b**		**8n**, 94	90
15[e]	**7a**	Ph	**2j**		**8o**, 85	90

[a] Reaction conditions unless otherwise specified: **7** (0.3 mmol), **2** (1.7 equiv), Me_2Zn (1.2 equiv), **3o** (5 mol%), toluene (1.2 mL), 19–48 h, 30 °C. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] With 2.5 equiv of **2**. [e] With 5.0 equiv of **2**.

and mild reaction conditions, we believe that this protocol will find applications in the synthesis of biologically active compounds, peptide design, and protein engineering.[22]

Experimental Section

General procedure for the catalytic enantioselective addition of terminal alkynes to ketoimines: Me_2Zn (1.2 equiv) was added to a solution of terminal alkyne **2** (1.7 equiv) in anhydrous toluene (1.2 mL) under argon at room temperature. After stirring for 1 h, the BINOL-type ligand (5 mol%) was added. The reaction mixture was stirred for 2.5 h at room temperature. The ketoimine (0.3 mmol) was then added. The reaction mixture was stirred at the same temperature until the starting material was fully consumed, as indicated by TLC. The reaction mixture was quenched with a solution of saturated NH_4Cl then diluted with EtOAc. The aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous sodium sulfate, and the solvent was removed. The residue was purified with column chromatography on silica gel to give the pure products.

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[17] CCDC 9342839 (**4d**), 9934284 (**5j**), 9934285 (**6j**), 9934286 (**7a**), and 9934287 (**9**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[18] The configuration of α-aryl α-imine esters **5** was assigned as *Z* by X-ray crystal structure analysis of **5j**, see the Supporting Information for details.

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[22] Editorial Note (further details to the inside cover graphic): The drawing depicts a well-known folklore in China named *Houyi She Ri* or *Houyi Shot Down Nine Suns*. In Chinese mythology, at around 2170 BC, there were ten suns in the sky. As a result, crops shriveled in the fields, lakes and ponds dried up, human and animals cowered in shelters or collapsed from exhaustion. Yao, the Emperor of China that time, decided to plead for divine intervention and to ask Houyi–the God of Archery–for help. So Houyi went to the shore of the East China Sea, lifted up his bow and shot down nine of the ten suns. As order was restored to the Earth, Houyi was hailed as a hero for mankind.

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