Chinese Chemical Letters Vol. 13, No. 10, pp 939 – 941, 2002
http://www.imm.ac.cn/journal/ccl.html

Diastereoselective and Enantioselective Synthesis of (1*S*, 2*S*)-2-Ethyl-1-aminocyclopropane Carboxylic Acid

Yi Bo ZHOU, Jun An MA, Li Xin WANG, Qi Lin ZHOU*

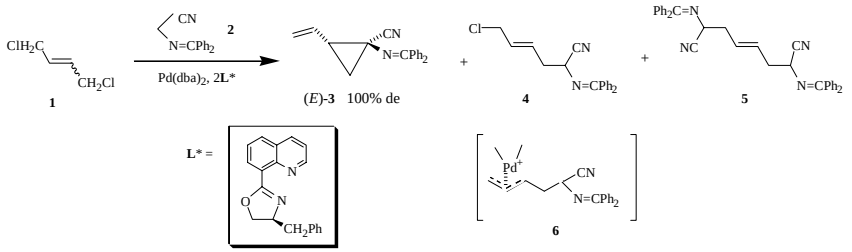
State Key Laboratoratory and Institute of Elemento-Organic Chemistry, Nankai University
Tianjin 300071

Abstract: Pd(0) Complex prepared from $Pd(dba)_2$ and chiral quinolinyl-oxazoline ligand can catalyze alkylation and cyclization reaction of 1, 4-dichlorobut-2-ene **1** with anion of N-(diphenylmethylene)amino acetonitrile **2** to provide (*E*)-2-ethenyl-1-N-(diphenylmethylene) amino cyclopropane carbonitrile **3** with 100% de and 20% ee. Reduction of (*E*)-**3** by diimide followed by acidic hydrolysis afforded (1*S*, 2*S*)-2-ethyl-1-aminocyclopropanecarboxylic acid **9**, a natural product *coronamic acid*.

Keywords: Chiral Pd catalyst, quinolinyl-oxazoline, cyclopropanecarboxylic acid.

During the last decade, 1-aminocyclopropanecarboxylic acid and its derivatives (ACCS) have attracted increasing attention of organic and bioorganic chemists due to their outstanding biological properties, ranging from antimicrobial, insecticidal, plant growth and fruit ripening controls, *etc*.[1]. Moreover, the three-membered carbocycle provides building blocks of unprecedented synthetic potential because it undergoes selective ring opening, ring enlargement or cycloaddition reactions[2]. The most exciting applications of ACCS are in the design and synthesis of conformationally constrained peptidometics[3]. Therefore development of stereoselective synthesis of this attractive class of compounds presented a challenging task of research.

Scheme 1



Approaches to diastereomerically and enantiomerically synthesis of ACCS involve

*E-mail: qlzhou@public.tpt.tj.cn

mainly chemical and enzymic resolution of racemic compounds or use of chiral auxiliaries in cyclopropanation reactions[3, 4]. So far, only a few papers reported the synthesis of ACCS using asymmetric catalytic strategy. Salaün[5] used Pd(0) complexes of (*S*)- and (*R*)-BINAP to catalyze the reaction of (*E, Z*)-1, 4-dichlorobut-2-ene **1** with N-(diphenylmethyleneamino)acetonitrile **2**, providing (*E*)-2-ethenyl-1-N-(diphenylmethylene) aminocyclopropane carbonitrile (*E*)-**3**, a suitable precursor of plant growth regulator *coronamic acid*. But the enantiomeric excess is lower than 5%[5]. We recently used chiral quinolinyl-oxazoline compounds as ligands in cyclopropanation[6], allylic oxidation[7] and Heck-type hydroarylation[8]. Herein, we report our investigation on the one-pot tandem alkylation and cyclization of 1, 4-dichlorobut-2-ene **1** with anion of N-(diphenylmethyleneamino)acetonitrile **2** catalyzed by Pd/quinolinyl-oxazoline complexes (**Scheme 1**).

Results and Discussions

To a 95 : 5 mixture of (*E*) and (*Z*)-1, 4-dichlorobut-2-ene **1** containing 0.05 equiv. of the palladium(0) complex prepared from $Pd(dba)_2$ and quinolinyl-oxazoline ligand (Pd/L* = 1 : 2) in THF, were added 1.2 equiv. of the nitrile **2** and 2 equiv. of NaH successively. The mixture was stirred at room temperature for 2 h to provide a diastereomerically pure (*E*)-2- ethenyl-1-N-(diphenylmethyleneamino)cyclopropane carbonitrile (*E*)-**3** with 71% yield (**Table 1**, entry 4), together with 17% dialkylation byproduct (*E*)-**5**. In the absence of Pd (0) catalyst, no reaction occurred. Replacement of the NaH by N, O-bis(trimethylsilyl)acetamide (BSA) gave (*E*)-**3** in lower than 5% yield (entry 1). Use of 1 equiv. of NaH remarkably increased the amount of byproduct **4** (entry 6). It must be underlined that the reaction of (*E, Z*)-**1** with **2** in the presence of 0.01 equiv. of Pd(0) catalyst gave a mixture of (*E*)-**3** (35%) and monoalkylated products **4** (26%) at room temperature for 2 h. After 3 days, however, monoalkylated products disappeared and (*E*)-**3** increased to 65% (entry 2). Increasing the amount of Pd(0) to 0.02 equiv., the reaction time could be shorten to 2.5 h .

It is obvious that the first step of the reaction is alkylation of allylic palladium intermediate with anion of diphenylmethyleneamino acetonitrile to afford monoalkylated products **4.** Intramolecular substitution of compound **4** to afford the final product **3** through an allylic palladium intermediate **6** in the precence of second eqiv. base. Low temperature led to slow intramolecular cyclization because conversion of **4** to (*E*)-**3** took a longer time (entry 5 *vs* entry 4). Moreover, the intramolecular attack of carbon

Table 1 Pd(0) catalyzed reaction of (*E, Z*)-**1** with aminoacetonitrile **2**

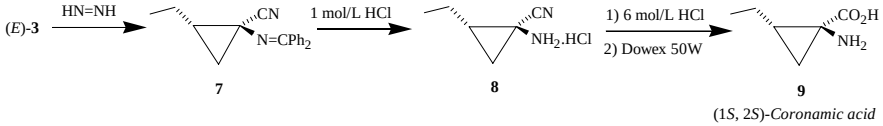
Entry	Pd(0)	Base	Temp.(°C)	Time	**3** (%)	**4** (%)	**5** (%)
1	0.05 eq.	BSA (2 eq.)	RT	65 h	<5	16	-
2	0.01 eq.	NaH (2 eq.)	RT	3 days	65	-	-
3	0.02 eq.	NaH (2 eq.)	RT	2.5 h	65	-	-
4	0.05 eq.	NaH (2 eq.)	RT	2 h	71	-	17
5	0.05 eq.	NaH (2 eq.)	0	17 h	63	<5	13
6	0.05 eq.	NaH (1 eq.)	0	17 h	18	30	12

anion in the intermediate **6** was completely stereoselective providing a sterrically favored *trans* isomer.

As a comparison, the chiral ligand (4*S*)-2-(2-diphenylphosphinophenyl)-4-isopropyl-oxazoline[9], which has been successful in various asymmetric reactions, was also tested in this tandem reaction, and only trace amount of desired product (*E*)-**3** (<2%) companied with 12 % of **4** was obtained after 10 h under reflux.

Reduction of (*E*)-**3** by diimide (prepared from azodicarboxylate, acetic acid and pyridine in methanol[5,10]) offered the saturated cyclopropane derivative 1-[(N-(diphenylmethylene)amino)-2-ethylcyclopropanecarbonitrile (*E*)-**7** in 85% yield (**Scheme 2**). Acidic hydrolysis of **7** with 1 mol/L HCl, followed by 6 mol/L HCl and then chromatography through a Dowex 50w×8-100 ion exchange column led to (1*S*, 2*S*)-*coronamic acid* **9** in 62% yield with an optical rotation of $[\alpha]_D^{20}$ + 6.47 (c 0.52, H_2O), the enantiomerical excess was 20%[11].

Scheme 2



In conclusion, one-pot tandem alkylation and cyclization of (*E*, *Z*)-1, 4-dichlorobut- 2-ene **1** with the benzophenone Schiff base **2** catalyzed by chiral palladium (0) complex of quinolinyl-oxazoline provided an efficient method for the preparation of cyclopropane derivative (*E*)-**3**, which is a key intermediate in the synthesis of natural product (1*S*, 2*S*)-*coronamic acid*.

Acknowledgment

We thank the National Natural Science Foundation of China, the Major State Basic Research Development Program (grant No. G2000077506), the Ministry of Education of China for the financial support.

References and Notes

1. For a review, see: J. Salaün, M. S. Baird, *Curr. Med. Chem*., **1995**, *2*, 511.
2. For a review , see: J. Salaün, *Top. Curr. Chem.*, Springor-Verlag Berlin, **1988**, *Vol. 144*, p1.
3. For recent review, see: K. Burgess, K. K. Ho, D. Moye-Sherman, *Synlett*, **1994**, 575.
4. For recent review, see: C. Cativiela, D. D. de Villegas, *Tetrhedron: Asymmetry*, **2000**, *11*, 645.
5. P. Dorizon, G. Su, R. Paugam, J. Ollivier, J. Salaün, *J. Org. Chem.*, **1999**, *64*, 4712.
6. X. Y. Wu, X. H. Li, Q. L. Zhou, *Tetrahedron: Asymmetry*, **1998**, *9*, 4143.
7. Z. P. Li, X. Y. Wu, Q. L. Zhou, *Chinese Journal of Chemistry*, **2001**, *19*, 40.
8. X. Y.Wu, H. D. Xu, Q. L. Zhou, A. S. C. Chan, *Tetrahedron: Asymmetry*, **2000**, *11*, 1255.
9. P. von Matt, A. Pfaltz, *Angew. Chem. Int. Ed. Engl.*, **1993**, *32*, 566.
10. U. Groth, W. Halfbrodt, U. Schollkopf, *Liebigs Ann. Chem*., **1992**, 351.
11. Calculated from the date $[\alpha]_D^{20}$ + 28 (c 0.50, H_2O, 88% ee) reported in: A. Gaucher, J. Ollivier, J. Marguerite, R. Paugam, J. Salaün, *Can. J. Chem*., **1994**, *72*, 1312.

Received 3 December, 2001