Sci. Bull. (2015) 60(2):210–215
DOI 10.1007/s11434-014-0708-5

www.scibull.com
www.springer.com/scp

Article

Chemistry

Copper(I)/SaBOX catalyzed highly diastereo- and enantio-selective cyclopropanation of *cis*-1,2-disubstituted olefins with α-nitrodiazoacetates

Liang-Wen Feng · Peng Wang · Lijia Wang · Yong Tang

Received: 19 November 2014 / Accepted: 13 December 2014 / Published online: 31 December 2014

Abstract A copper-catalyzed highly stereoselective cyclopropanation of 1,2-disubstituted olefins with α-nitrodiazo acetates has been developed, giving the desired products in up to 97 % yields, up to >99/1 dr and up to 98 % ee, which provides an efficient access to the synthesis of optical active cyclopropane α-amino acids and unnatural α-amino acid derivatives.

Keywords Asymmetric catalysis · Cyclopropanation · Sidearm · Bisoxazoline · α-Amino acids

1 Introduction

Nitrocyclopropane carboxylates are an important class of compounds that are suitable precursors of biologically important cyclopropane α-amino acids [1, 2] as well as various unnatural α-amino acid derivatives that could be easily accessed by ring-opening transformations [3, 4]. One of the most effective methods for the stereoselective synthesis of nitrocyclopropane carboxylates is the transition-metal-catalyzed asymmetric cyclopropanation of olefins with nitrodiazoacetates [5–7]. However, like other diacceptor diazo compounds, the nitrodiazoacetate was inherently less reactive to form metal carbene [8–23]. Charette and co-workers developed an efficient access to disubstituted α-nitrocyclopropyl ketones by using chiral rhodium(II) carboxylate as catalyst, in which 54 %–91 % yields, 94/6–99/1 dr and 87 %–95 % ee were achieved [6]. Zhang and co-workers [7] succeeded in the chiral radical cobalt/porphyrin complex-catalyzed asymmetric *Z*-cyclopropanation of both electron-rich and electron-deficient terminal alkenes with α-nitrodiazoacetates under carbene radical process (42 %–97 % yields, 53/47–>99/1 and 75 %–95 % ee). When copper was used as catalyst, harsh conditions such as elevated temperature [24, 25] and extra activator [5] are required, but both the reactivity and stereoselectivity are unsatisfactory. For example, Charette and Wurz [5] found that compared with Rh(II) catalysts, the Cu(I)-bisoxazoline (BOX) catalysts were less reactive in the cyclopropanation of styrene with nitrodiazoacetate, and up to 55 % yield and up to 72 % ee were obtained. Later on, they [26] successfully realized asymmetric cyclopropanation of terminal alkenes in 45 %–84 % yields with 82/18–95/5 dr and 68 %–93 % ee by employing iodonium ylides [26–29] as carbene sources. To date, less active 1,2-disubstituted olefins [30, 31] have barely been employed in this reaction, except one example of indene substrate was reported in 72 % yield, 95/5 dr and 98 % ee after recrystallization [28]. Herein, we wish to report our recent efforts on the asymmetric cyclopropanation of *cis*-1,2-disubstituted olefins with α-nitrodiazoacetates by using copper(I)/SaBOX as catalyst.

Liang-Wen Feng and Peng Wang have contributed equally to this work.

Electronic supplementary material The online version of this article (doi:10.1007/s11434-014-0708-5) contains supplementary material, which is available to authorized users.

L.-W. Feng · P. Wang · L. Wang · Y. Tang (✉)
The State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China
e-mail: tangy@sioc.ac.cn

Y. Tang
Collaborative Innovation Center of Chemical Science and Engineering, Tianjin 300072, China

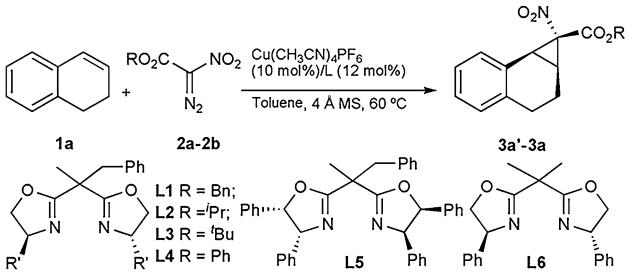
2 Materials and methods

Typical procedure for the asymmetric cyclopropanation (**3a** as an example): A mixture of $Cu(MeCN)_4PF_6$ (0.04 mmol) and the ligand (**L5**, 0.048 mmol) in toluene (3 mL) with activated 4 Å molecular sieve (MS) was stirred at 50 °C for 2 h under an atmosphere of nitrogen. Then, **1a** (2.0 mmol) and diazo **2b** (0.4 mmol) were added to the mixture of catalyst via microsyringes, followed by washing with 1 mL toluene. The resulting suspension was allowed to stir at 50 °C. After the reaction was complete (monitoring by thin-layer chromatography), the reaction was filtered through a glass funnel with a thin layer (20 mm) of silica gel (100–200 mesh) with CH_2Cl_2 (~30 mL). The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/petroleum, 1/80) to afford **3a** as white solid in 85 % with >99/1 dr and 98 % ee (determined by high-performance liquid chromatography (HPLC) analysis: chiralcel OD-3 column (25 cm), heptane/*i*-PrOH = 99/1, 1.0 mL/min, 254 nm; tr (major) = 10.4 min, tr (minor) = 12.4 min); $[\alpha]_D^{20} = +65.6°$ (c = 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.34 (m, 1H), 7.22–7.17 (m, 2H), 7.05–7.02 (m, 1H), 4.16–3.99 (m, 2H), 3.32 (d, J = 10.4 Hz, 1H), 2.94–2.89 (m, 1H), 2.76–2.69 (m, 1H), 2.44–2.32 (m, 2H), 2.17–2.07 (m, 1H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 134.5, 130.7, 128.7, 128.5, 127.8, 126.6, 73.2, 62.4, 32.5, 29.8, 25.0, 16.9, 13.3; IR (neat, cm^{-1}): 2,986, 2,938, 1,739, 1,537, 1,335, 1,184, 1,107, 1,089, 1,019, 796, 755, 730, 687; HRMS-ESI: $[M+H]^+$ Calcd. for $C_{14}H_{16}NO_4$, 262.1079; Found, 262.1076.

3 Results and discussion

Recently, we have developed a series of sidearm-modified bisoxazoline ligands (SaBOX), which could improve the reactivity and stereoselectivity in the asymmetric cyclopropanation of multisubstituted olefins with diazoacetates [32, 33]. Thus, we tried to extend this strategy to the asymmetric cyclopropanation of 1,2-disubstituted olefins with α-nitrodiazoacetates. Initially, the study was carried out in toluene at 60 °C under nitrogen atmosphere using dialin **1a** and methyl nitrodiazoacetate **2a** as starting material. With phenyl-sidearmed SaBOX **L1**, when $Cu(MeCN)_4PF_6$/**L1** was employed as catalyst, the reaction proceeded slowly, furnishing the nitrocyclopropane **3a** in only 9 % yield with >99/1 dr and 94 % ee after 24 h (Table 1, entry 1). In order to further increase the yield, several SaBOX ligands bearing different substituents on the oxazoline backbone were then examined. With *iso*propyl group, **L2** gave 14 % yield (entry 2), while with

Table 1 Reaction optimization[a]



Entry	Ligand	R	Time (h)	Yield (%)[b]	dr[c]	ee (%)[d]
1	**L1**	Me	24	9	>99/1	94
2	**L2**	Me	24	14	>99/1	95
3	**L3**	Me	24	Trace	–	–
4	**L4**	Me	11	66	>99/1	97
5	**L5**	Me	3	80	>99/1	97[e]
6[f]	**L5**	Me	6	81	>99/1	98[e]
7[f,g]	**L5**	Me	2.5	81	>99/1	98[e]
8[f]	**L5**	Et	3	85	>99/1	98[e]
9[f,g]	**L6**	Et	3	15	>99/1	86

[a] **1/2** = 5/1 and [**2**] = 0.1 mol/L in toluene (4 mL) with 4 Å MS under N_2 at 60 °C. [b] Isolated yields; [c] determined by ^1H NMR analysis; [d] determined by chiral HPLC; [e] the enantioselectivity is reversed; [f] at 50 °C; [g] with CuI (10 mol%) and $AgSbF_6$ (12 mol%)

tert-butyl group, **L3** led to only trace cyclopropanation product (entry 3). Then, we attempted to use *L*-phenylglycine-derived **L4** as ligand. To our delight, the reactivity was promoted obviously giving the desired product **3a′** in 66 % yield after 11 h; meanwhile, the enantioselectivity was also raised slightly with 97 % ee (entry 4). After an extensive screening of SaBOX ligands (see Supporting information, online), **L5** derived from 2-amino-1,2-diphenylethanol was emerged as the best ligands, which speeded up the reaction sharply and accomplished 80 % yield within 3 h without any erosion of the stereocontrol but the reversed enantioselectivity (entry 5). Lowering the reaction temperature from 60 to 50 °C increased the ee to 98 %, but it needs 6 h to finish the reaction (entry 6). In addition, $CuSbF_6$ proved also to be a more efficient metal salt and 81 % yield, >99/1 dr and 98 % ee was obtained in only 2.5 h, with **L5** as ligand (entry 6 vs. entry 7). Changing the ester group of nitrodiazoacetate from methyl **2a** to ethyl **2b**, leading to a little bit of improvement in the yield of **3a** with maintenance of the stereoselectivity after 3 h (85 % yield, >99/1 dr and 98 % ee, entry 8). However, as to BOX ligand [34–39] **L6**, which proved very efficient in the asymmetric cyclopropanation of terminal olefin with iodonium ylides [26], only gave 30 % yield of **3a** after 3 h even in the presence of more active $CuSbF_6$ (entry 6 vs. entry 7), indicating that the SaBOX ligand is more efficient (entry 8 vs. entry 9).