Tetrahedron 71 (2015) 8585–8592

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Chiral recyclable fluorous disulfonamide ligand for catalytic enantioselective cyclopropanation of allylic alcohols

Yuya Kawashima [a], Tetsuya Ezawa [a], Mai Yamamura [a], Taisuke Harada [a], Takuya Noguchi [a], Tsuyoshi Miura [b], Nobuyuki Imai [a,*]

[a] Faculty of Pharmacy, Chiba Institute of Science, 15-8 Shiomi-cho, Choshi, Chiba 288-0025, Japan
[b] Tokyo University of Pharmacy and Life Sciences, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

ARTICLE INFO

Article history:
Received 7 July 2015
Received in revised form 5 September 2015
Accepted 10 September 2015
Available online 11 September 2015

Keywords:
Enantioselectivity
Simmons–Smith cyclopropanation
Fluorous disulfonamide
Chiral ligand
Recycle

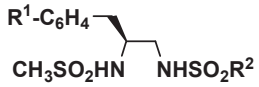
ABSTRACT

Allylic alcohols reacted with Et_2Zn and CH_2I_2 in the presence of a catalytic amount of fluorous disulfonamide **3a** to afford the corresponding cyclopropylmethanols in 69%-quantitative yields with 49–85% ee. Recovery of the fluorous ligand **3a** was readily performed from the reaction mixture by the fluorous solid-phase extraction (FSPE), and the recovered **3a** could be reused without a significant loss of the catalytic activity and enantioselectivity.

1. Introduction

Horváth and Rabái have initially developed fluorous recovering technique in the field of catalytic chemistry,[1] then Curran has established the fluorous solid-phase extraction (FSPE) methodology using fluorous silica gel.[2] Asymmetric reactions by FSPE concept for recovery and reuse of the expensive chiral ligands have also been reported.[3]

Furthermore, enantioselective cyclopropanations using chiral ligands are very attractive owing to various kinds of bioactivities in the possession of cyclopropane derivatives,[4] and some effective methods for catalytic enantioselective Simmons–Smith cyclopropanations have been reported since Kobayashi developed the first and unique reaction.[5] We have recently reported that the catalytic enantioselective Simmons–Smith cyclopropanations using L-phenylalanine-derived disulfonamides (**1** and **2**) as a chiral ligand afforded the corresponding cyclopropylmethanols in 82%-quantitative yields with 39–86% ee.[6]



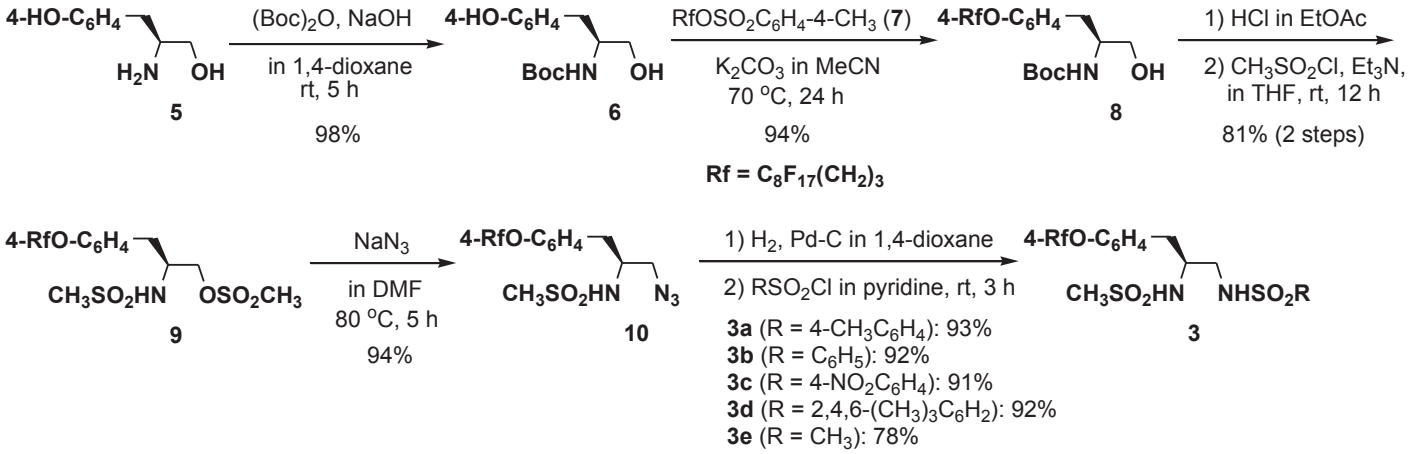
1: R^1 = H, R^2 = 4-$NO_2C_6H_4$
2: R^1 = H, R^2 = 4-$CH_3C_6H_4$
3: R^1 = $C_8F_{17}(CH_2)_3O$,
R^2 = 4-$CH_3C_6H_4$, C_6H_5, 4-$NO_2C_6H_4$,
2,4,6-$(CH_3)_3C_6H_2$, CH_3
4: R^1 = H, R^2 = C_8F_{17}

2. Results and discussion

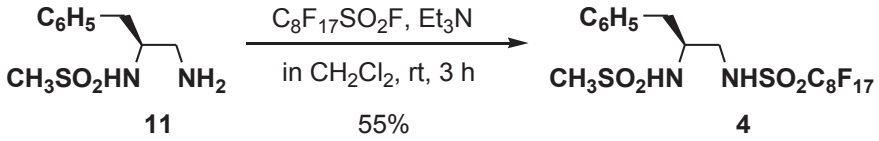
To recover and reuse the valuable ligands such as **1** and **2** for enanitoselective Simons–Smith cyclopropanation, we have developed the fluorous disulfonamides **3** as a novel chiral ligand with fluorous tag.[7] It is suggested that a fluorous chain should be introduced into a distant position from the two sulfonamides and that the distance is important for the enantioselectivity.[6d] Herein, we describe the detail of the catalytic enantioselective cyclopropanation using recyclable fluorous disulfonamides **3** as a chiral ligand.

* Corresponding author. E-mail address: nimai@cis.ac.jp (N. Imai).

http://dx.doi.org/10.1016/j.tet.2015.09.024
0040-4020/



Scheme 1. Preparation of the fluorous disulfonamides **3**.



Scheme 2. Preparation of the fluorous disulfonamide **4**.

The fluorous disulfonamides **3** were initially designed as a novel recyclable chiral ligand (see Scheme 1). The amino group of L-tyrosinol **5** was protected by *t*-butoxycarbonyl (Boc) group to give the corresponding alcohol **6** in 98% yield. The reaction of **6** with the fluorous tosylate **7**[8] in the presence of potassium carbonate in acetonitrile provided the fluorous alcohol **8** in 94% yield. The Boc group of **8** was removed by treatment with hydrogen chloride in ethyl acetate, followed by the reaction with methanesulfonyl chloride (MsCl) in tetrahydrofuran (THF) to afford 81% yield of the corresponding mesylate **9** in two steps. The azide **10** was obtained in 94% yield by the reaction of **9** with sodium azide in *N*,*N*-dimethylformamide (DMF). The azide **10** was hydrogenated in the presence of Pd on carbon in 1,4-dioxane, followed by the reaction of 4-toluenesulfonyl chloride (TsCl) in pyridine to provide 93% yield of the desired fluorous disulfonamide **3a** in two steps. In addition to fluorous disulfonamide **3a**, various fluorous disulfonamides **3b**–**3e** were prepared in excellent yields. Fluorous disulfonamide **4** containing a fluorous chain on the sulfonamide part was prepared as shown in Scheme 2. The amine **11** as the intermediate for synthesis of chiral ligand **2** was easily prepared from L-phenylalaninol through two steps.[6]

We optimized the reaction conditions for enantioselective cyclopropanation as shown in Table 1. The various reaction temperatures from −23 °C to 10 °C were examined in the presence of the fluorous disulfonamide **3a** (0.1 equiv) in anhydrous dichloromethane (see entries 1–6). The more suitable reaction temperature was 0 °C as indicated in entry 4. The cyclopropanation was carried out with 0.2 and 0.3 equiv of the fluorous disulfonamide **3a** to afford 78% and 79% ee, respectively (see entries 7 and 8). This reaction was performed for 3 h to 0 °C or for 23 h to −23 °C with fluorous disulfonamide **4** containing fluorous chain on the sulfonamide part to afford 9% and 31% ee, respectively (see entries 9 and 10). It is guessed that the fluorous chain on the position of the sulfonamide part is not suitable by the disappearance of the π-π stacking effect.

Next, we examined the various fluorous disulfonamides **3** as a chiral ligand for enantioselective cyclopropanation as shown in Table 2. The disulfonamides **3a**–**3d** substituted by 4-toluenesulfonyl, benzenesulfonyl, 4-nitrobenzenesulfonyl, and methanesulfonyl gave good enantioselectivities (see entries 1–3, 5). A poor enantioselectivity 35% ee was obtained in the cyclopropanation in the presence of the disulfonamide **3d** containing a sterically bulky substituent such as 2,4,6-trimethylbenzenesulfonyl group (see entry 4). We selected the fluorous disulfonamide **3a** as the optimized chiral ligand because it is possible to be more easily and cheaply prepared, and high enantioselectivities were obtained in the catalytic enantioselective cyclopropanation of allylic alcohols using **3a** as well as using the known disulfonamide **2**.[6]

The results of enantioselective cyclopropanation of various allylic alcohols **12a**–**12p** in the presence of 0.2 equiv of **3a** are shown in Table 3. We selected methoxy and methyl substituents as representative electron-donating groups (see entries 2–5), then trifluoromethyl, chloro, and bromo substituents as electron-withdrawing groups (see entries 6–10) on the benzene ring. The reaction of the cinnamyl alcohol **12f** substituted with trifluoromethyl group afforded the highest enantioselectivity (83% ee) among those of 4-substituted cinnamyl alcohols (see entries 2, 3, 6, 7, 10, 11). In the case of the reactions of cinnamyl alcohols substituted with methyl and chloro groups (see entries 3–5 and 7–9), 2-substituted cinnamyl alcohols **12e** and **12i** afforded higher enantioselectivities (75% ee and 85% ee, respectively) than 4- and 3-substituted cinnamyl alcohols **12c**, **12d** and **12g**, **12h**. Then, a lower enantioselectivity 54% ee was obtained in the reaction using 2,4,6-trisubstituted cinnamyl alcohol **12k** (see entry 11). The other *trans*-oriented allylic alcohols **12l**–**12n** were converted to the corresponding derivatives in excellent yields with 67–74% ee. The lowest enantioselectivity 49% ee was obtained in the reaction of the *cis*-oriented allylic alcohol **12o** due to the steric hindrance between the allylic alcohol **12o** and the ligand **3a** (see entry 15). The reaction of 3,3-diphenyl-2-propen-1-ol **12p** afforded 71% ee (see entry 16) to afford the corresponding cyclopropanemethanol **13p**, which is easily converted to (*R*)-(+)-cibenzoline.[6a,b]

Furthermore, the fluorous ligand makes it possible to recover itself using fluorous silica gel based on solid-phase extraction. The fluorous disulfonamide **3a** was cleanly recovered (>92%) from the