Introduction

Nowadays there is more and more interest in organocatalysis, due to its low toxicity and good selectivity compared to the traditional metal-based catalysis. Organocatalysis also reflects many requirements of green chemistry. Therefore, many of chemists focus on this field, trying to find some efficient and operationally simple organocatalysts. Many wonderful works were reported and some of them were of great importance. In this paper, we tried to apply the concept of organocatalysis [1–12]. Also, inspired by the fluorous-tagging idea, we prepared recyclable organocatalysts fluorous hydrazine-1,2-bis(carbothioate) 1 and hydrazine-1,2-dicarboxylate 2 (Scheme 1) and then applied them to the synthesis of β-chloroethers under mild reaction conditions [7–9]. The catalytic reaction proceeded smoothly, and with the aid of fluorous silica gel, these fluorous compounds could be recovered easily by fluorous solid-phase extraction (F-SPE) and no environmentally harmful perfluoro-solvents were used [13–22].

Scheme 1. Fluorous organocatalysts 1 and 2.

Results and Discussion

The synthetic routes for creating the fluorous organocatalysts (1 and 2) are illustrated in Scheme 2. First, 1,1′-(thio)carbonyl diimidazole I and 2-perfluoroethyl ethanol II were mixed and stirred in
CH$_2$Cl$_2$ at room temperature. Then, quenching with H$_2$O and extraction with petroleum ether afforded crude product III, and compound III was purified in a silica column, and then reacted with Et$_3$N and NH$_2$NH$_2$-HCl. Fluorous hydrazine-1,2-bis(carbothioate) 1 and hydrazine-1,2-dicarboxylate 2 were isolated as white powders.

![Scheme 2](image)

**Scheme 2.** Synthetic route of fluorous hydrazine-1,2-bis(carbothioate) 1 and hydrazine-1, 2-dicarboxylate 2. (DCM: dichloromethane).

The reaction of styrene with NCS (N-Chlorosuccinimide) in methanol was selected as the model reaction for further investigation (Table 1). Different catalysts, catalyst loading, reaction times and quantitative rations of NCS were investigated. It was a slow and low-yield process with no catalyst employed in the model reaction (Table 1, entry 1). We tried the fluorous catalysts 1 and 2 in this catalytic reaction and found catalyst 1 was the more efficient structure for promoting the synthesis compared to 2 as the reaction catalyst (Table 1, entries 6 and 8). Catalyst loading and the quantitative rations of NCS were also studied (Table 1, entries 2–7), and when economy, reaction speed and reaction yield were all evaluated, entry 6 was considered as the optimal reaction condition for this catalytic reaction.

<table>
<thead>
<tr>
<th>Entry</th>
<th>NCS (mmol)</th>
<th>Catalyst (mol %)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>-</td>
<td>120</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>1 (20)</td>
<td>1</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1 (10)</td>
<td>1</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>1 (5)</td>
<td>2</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
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<tr>
<td>6</td>
<td>2</td>
<td>1 (5)</td>
<td>2</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>1.5</td>
<td>1 (5)</td>
<td>4</td>
<td>68</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>2 (5)</td>
<td>48</td>
<td>33</td>
</tr>
</tbody>
</table>

* The reaction condition: styrene (1 mmol); MeOH (3 mL); 25 °C; NCS (N-Chlorosuccinimide).

Next, various alcohols and alkenes were employed in this reaction for observation (Table 2). A lower yield and slower reaction rate was observed when methanol was replaced with ethanol (Table 2, entry 2). When pentan-3-ol, t-butanol and phenol were used as substrates in this catalytic reaction, it gave a much slower reaction with only a moderate yield (Table 2, entries 3–5). When the para position of styrene was substituted with a methyl or chlorine group, the reaction afforded an excellent yield of product with a slower reaction rate (Table 2, entries 6 and 7). We did not get the correct product when we used 2-chlorostyrene or 3-chlorostyrene. Digeminal-substituted olefin offered a faster reaction with an excellent yield (Table 2, entry 8). Cyclohexene was also investigated, and
it gave a moderate yield. Moreover, the product was completely stereocontrolled (Table 2, entry 9). We also tried aliphatic alkenes (1-octene and 1-decene); however, the yields were too low to detect.

**Table 2.** Compound 1 catalyzed the synthesis of β-chloroether of variety of olefins and alcohols a.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Olefin</th>
<th>ROH</th>
<th>Reaction Time (h)</th>
<th>Chloride</th>
<th>Yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>MeOH</td>
<td>2</td>
<td></td>
<td>81</td>
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<tr>
<td>2</td>
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</tr>
<tr>
<td>9</td>
<td>1</td>
<td>MeOH</td>
<td>0.5</td>
<td></td>
<td>52</td>
</tr>
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</table>

*a* Olefin (1 mmol), NCS (2 mmol), 1 (5 mol %) and ROH 3 mL, 25 °C.

We speculated that a possible key step in this synthesis of the β-chloroether reaction with NCS may include hydrogen bonding, as shown in Figure 1. Polar protic solvents or reactants could help to get a strong hydrogen bond network.
We also did catalyst recycling experiments using a model reaction; the fluorous catalyst 1 could be easily recovered up to three times by F-SPE using fluorous silica gel with an excellent catalyst to recover the purity and a good recycling yield (Figure 2).

3. Experimental Section

3.1. General

The Nuclear Magnetic Resonance (NMR) spectra are recorded by spectrometer (Bruker Advance RX500, Bruker, Billerica, MA, USA). And β-chloroether compounds are synthesized and compared to the spectra which are reported by related literature. The substrates and reagents are commercial available and are used without further purification.

3.2. The Synthesis of Fluorous Catalyst 1

To a solution of compound I (1.958 g, 11 mmol) in anhydrous dicholomethane, 3.641 g (10 mmol) II was added slowly. The mixture was kept stirring at 25 °C for 12 h, after quenched with water, the mixture was extracted with 50 mL petroleum ether for three times. After removal the solvent and dry the residue. The crude compound III was taken up in 50 mL tetrahydrofuran. Compound III was purified in silica column, then reacted with Et₃N (2.529 g, 25 mmol) and NH₂NH₂∙HCl (0.342 g, 5 mmol) at 25 °C for seven days. The fluorous hydrazine-1,2-bis(carbothioate) I (2.363 g, 56%) was isolated as white powder: Mass Spectrometer (Electron Spray Ionization+) m/z 843.00 (M−H); ¹H NMR (500 MHz, CD₃OD): δ 4.83–4.76 (m, 4H), 2.78–2.60 (m, 4H); ¹⁹F NMR: δ −82.5 (6F), −114.5 (4F), −122.9
3.3. The Synthesis of β-Chloroethers Catalyzed by 1 and the Catalyst Recycling Experiment

To a solution of 0.267 g (2 mmol) N-chlorosuccinimide and 0.042 g (0.05 mmol) catalyst 1 in 3 mL methanol, 1 mmol olefin was added and kept stirring at room temperature for 0.5–48 h. FluoroFlash® silica gel cartridge (5 g) was used for separation. The reaction mixture was loaded onto this silica gel. First, eluted by 80% methanol for non-fluorous components, then concentrated for column chromatography to provide corresponding β-chloroethers products. Diethyl ether was then used to wash out the fluorous compound 1. After removal the solvent, the fluorous catalyst 1 could be used for the next run.

4. Conclusions

In conclusion, we prepared a fluorous organocatalyst for the β-chloroether reaction with NCS; the fluorous catalyst exhibited good catalytic activity. This fluorous organocatalyst could also be easily recycled three times with F-SPE.

Supplementary Materials: The following are available online at www.mdpi.com/2073-4344/7/2/66/s1, Figures S1–S3, 1H NMR, 13C NMR and 13C NMR of the fluorous hydrazine-1,2-bis(carbothioate) 1.

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Author Contributions: Yi-Wei Zhu conceived of and designed the experiments. Yu-Qi Yin performed the experiments. Yu-Qi Yin and Yi-Xin Shi analyzed the experimental data.

Conflicts of Interest: The authors declare that they have no conflict of interest to this work.

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