**Perfluoroalkanesulfonamide Organocatalysts for Asymmetric Conjugate Additions of Branched Aldehydes to Vinyl Sulfones**

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**Abstract:** Asymmetric conjugate additions of branched aldehydes to vinyl sulfones promoted by sulfonamide organocatalyst 6 or 7 have been developed, allowing facile synthesis of the corresponding adducts with all-carbon quaternary stereocenters in excellent yields with up to 95% ee.

**Keywords:** organocatalyst; sulfonamide; vinyl sulfone; conjugate addition; quaternary stereocenters; fluorous

1. Introduction

All-carbon quaternary stereocenters are one of the most important motifs in many natural products and bioactive compounds; however, relatively harsh reaction conditions are required to construct these stereocenters due to their steric hindrance. In addition, combinations of electrophile and nucleophile are limited, and the stereoselective construction of all-carbon quaternary stereocenters is not generally straightforward. Therefore, development of efficient synthetic methods to stereoselectively construct all-carbon quaternary stereocenters under mild reaction conditions is highly desirable in organic synthesis [1–13]. Among various methodologies to construct these centers, organocatalysis is one of the most effective processes that can be performed under mild conditions. The synthetic methods for compounds with quaternary stereogenic centers using organocatalysts have received considerable
attention, particularly in the field of green chemistry [14,15]. Michael additions of various carbonyl compounds to 1,1-bis(benzenesulfonyl)ethylene (11) using organocatalysts are efficient synthetic methods, and several research groups have reported findings in this area [16–33]; however, successful conjugate additions of α-branched aldehydes and 11 for the construction of such all-carbon quaternary stereocenters have been rarely reported [34–38]. Alexakis and coworkers reported that L-proline derivatives catalyze the reaction of 11 with α-branched aldehyde 12a to give the corresponding adduct 13a with up to 73% ee [34,35]. Lu and coworkers reported that the sulfonamide organocatalyst derived from L-threonine promotes the conjugate addition of 12a to 11 in the unusual reaction solvent p-fluorotoluene to afford the corresponding adduct 13a in high yield with high enantioselectivity (up to 83% ee) [36]. Furthermore, Maruoka and coworkers reported efficient conjugate additions of α-heterosubstituted aldehydes with 11 using a sulfonamide organocatalyst with a dihydroanthracene framework (up to 95% ee) [37]. Recently, we also reported that a diaminomethylenemalononitrile organocatalyst catalyzes similar conjugate additions to afford 13a with high enantioselectivity (up to 89% ee) [38].

On the other hand, fluororous compounds with a perfluoroalkyl group can be easily separated from nonfluorous compounds by fluororous organic solvent extraction or fluororous solid phase extraction (FSPE) using fluororous silica gel [39]. Several research groups have reported asymmetric reactions in which fluororous organocatalysts are recyclable [40]. We have also reported a direct aldol reaction in water using fluororous sulfonamide organocatalyst 3 and related catalysts [41–43], Michael addition reactions using a fluororous thiourea organocatalyst [44], and an oxidation reaction using fluororous IBX [45]. In addition, we have reported a method for the synthesis of both enantiomeric aldol products in water using sulfonamide organocatalysts 1 [46] and 2 [47,48], prepared from L-phenylalanine. Very recently, we reported in a preliminary communication that perfluoroalkanesulfonamides 5 and 6 catalyze the conjugate additions of branched aldehydes to vinyl sulfone 11 to give the corresponding adducts with excellent stereoselectivities [49]; however, development of a protocol for recovery and reuse of 5 and 6 is yet to be reported. Herein, we describe the full details of the conjugate additions of branched aldehydes to vinyl sulfone using 6 and novel fluororous sulfonamide 7 (Figure 1).

![Figure 1. Structure of organocatalysts.](image)

2. Results and Discussion

We initially examined the sulfonamide organocatalysts 1–7 for the conjugate addition of 12a to 11 as a test reactant (Table 1). Sulfonamide organocatalysts 1–4 derived from L-phenylalanine were superior to catalyst 5 derived from L-valine for the direct aldol reactions in water [37,46,48]; however, 5 bearing the valine skeleton resulted more suitable for the conjugate addition with vinyl sulfone 11 (entries 1–5). Furthermore, to develop a more powerful organocatalyst, we synthesized 6, which
enhanced the acidity of the sulfonamide group by the introduction of the perfluorobutyl group. Treatment of compound 8 [50] with perfluorobutanesulfonyl fluoride in presence of triethylamine in dichloromethane provided the intermediate 9 in 79% yield. The Boc protective group was removed by treatment of hydrogen chloride in ethyl acetate to give the desired perfluorobutanesulfonamide 6 in 90% yield (Scheme 1). Organocatalyst 6 was more effective for conjugate additions with vinyl sulfone 11, resulting in the highest enantioselectivity (91% ee) and excellent yield (entry 6). Furthermore, to develop an organocatalyst that can be recovered and reused, 7 was synthesized by a similar procedure (Scheme 2). The stereoselectivity was slightly reduced in the reaction using 7 (entry 7).

### Table 1. Selection of organocatalyst.

| Entry | Catalyst | Time (h) | Yield a (%) | ee b (%) |
|-------|----------|----------|-------------|----------|
| 1     | 1        | 1        | 95          | -2       |
| 2     | 2        | 1.5      | 99          | 80       |
| 3     | 3        | 2        | 88          | 86       |
| 4     | 4        | 2        | 97          | 79       |
| 5     | 5        | 2        | 95          | 88       |
| 6     | 6        | 2        | 100         | 91       |
| 7     | 7        | 2        | 99          | 89       |

*a isolated yield; b determined by HPLC analysis.

### Scheme 1. Preparation of organocatalyst 6.

### Scheme 2. Preparation of organocatalyst 7.

We investigated the optimal reaction conditions for the enantioselective conjugate additions using 6, various solvents, and additives (Table 2). Conjugate additions were performed with vinyl sulfone 11 and 2-methylphenylethanal (12a) as test reactants in the presence of a catalytic amount of 6 and trifluoroacetic acid (TFA) at room temperature. A slight reduction in enantioselectivity and much longer reaction time were observed without TFA (entries 1 and 2). Aprotic solvents such as dichloromethane, diethyl ether, ethyl acetate, acetonitrile, chloroform, 1,2-dichloroethane, and p, m, and o-xylene were accepted well in this conjugate addition with good enantioselectivity (entries 3 and 5–12). A protic polar solvent such as methanol is a poor solvent for this reaction and provided low yield and enantioselectivity (entry 4). Among the solvents probed, the best results (95% yield and 93% ee) were
achieved when the reaction was performed in \( m \)-xylene (entry 11). We also examined the effects associated with the presence of other protic acids, including benzoic acid, \( p \)-nitrobenzoic acid, and trifluoromethanesulfonic acid; however, TFA was found to be the most suitable additive (entries 13–15). Additions of 0.2 or 0.05 equiv of TFA resulted in a slight reduction in stereoselectivity (entries 16 and 17). The highest enantioselectivity (95% ee) was obtained when the reaction was performed at 0 °C or −10 °C, although longer reaction time (21 h or 72 h) was required (entries 18 and 19). Enantioselectivity was slightly reduced when the catalyst loading was lowered to 0.05 equiv (entry 20). Considering the reaction time, the optimal conditions were determined to be 0.1 equiv of 6 and 0.1 equiv of TFA in \( m \)-xylene at room temperature (entry 11).

### Table 2. Optimization of reaction conditions using organocatalyst 6.

| Entry | Solvent     | Temp | Additive (equiv) | Time (h) | Yield \(^a\) (%) | ee \(^b\) (%) |
|-------|-------------|------|------------------|---------|-----------------|-------------|
| 1     | toluene     | rt   | none             | 24      | 75              | 86          |
| 2     | toluene     | rt   | TFA (0.1)        | 2       | 100             | 91          |
| 3     | CH\(_2\)Cl\(_2\) | rt   | TFA (0.1)        | 2.5     | 97              | 91          |
| 4     | MeOH        | rt   | TFA (0.1)        | 24      | 33              | 32          |
| 5     | Et\(_2\)O   | rt   | TFA (0.1)        | 5       | 87              | 82          |
| 6     | EtOAc       | rt   | TFA (0.1)        | 2.5     | 98              | 86          |
| 7     | MeCN        | rt   | TFA (0.1)        | 4       | 87              | 77          |
| 8     | CHCl\(_3\)  | rt   | TFA (0.1)        | 2       | 99              | 91          |
| 9     | ClCH\(_2\)CH\(_2\)Cl | rt   | TFA (0.1)        | 2       | 98              | 92          |
| 10    | \( p \)-xylene | rt   | TFA (0.1)        | 2       | 94              | 92          |
| 11    | \( m \)-xylene | rt   | TFA (0.1)        | 2       | 95              | 93          |
| 12    | \( o \)-xylene | rt   | TFA (0.1)        | 2       | 97              | 89          |
| 13    | \( m \)-xylene | rt   | PhCO\(_2\)H (0.1) | 5.5     | 46              | 80          |
| 14    | \( m \)-xylene | rt   | 4-NO\(_2\)C\(_6\)H\(_4\)CO\(_2\)H (0.1) | 24      | 85              | 82          |
| 15    | \( m \)-xylene | rt   | TiOH (0.1)       | 24      | 24              | 83          |
| 16    | \( m \)-xylene | rt   | TFA (0.2)        | 2       | 97              | 91          |
| 17    | \( m \)-xylene | rt   | TFA (0.05)       | 2       | 98              | 91          |
| 18    | \( m \)-xylene | 0 °C | TFA (0.1)        | 21      | 99              | 95          |
| 19    | \( m \)-xylene | \( -10 \)°C | TFA (0.1)    | 72      | 94              | 95          |
| 20    | \( m \)-xylene | rt   | TFA (0.05)       | 3       | 99              | 90          |
| 21    | \( m \)-xylene | rt   | TFA (0.01)       | 20      | 96              | 89          |

\(^a\) Isolated yield; \(^b\) Determined by HPLC analysis; \(^c\) Catalyst (0.05 equiv) was used; \(^d\) Catalyst (0.01 equiv) was used.

In order to identify the scope and limitations of aldehyde substrates, we investigated substituent effects of the branched aromatic aldehydes on the conjugate additions (Table 3). A range of electron-withdrawing substituents such as bromo and fluoro moieties, and electron-donating substituents such as methyl and methoxy groups on the aromatic ring of branched aldehydes \( 12b-g \) provided the corresponding adducts in excellent yields with good enantioselectivities (83%–92% ee) (entries 2–7). The additions of branched aldehydes possessing a naphthalene motif, \( 12h \) and \( 12i \), to vinyl sulfone \( 11 \) proceeded smoothly in the presence of a catalytic amount of 6 to afford the corresponding adducts \( 13h \) and \( 13i \) in
excellent yields with 92% ee, respectively (entries 8 and 9). Interestingly, 2-methoxy-2-phenylacetaldehyde (12j) was also applicable and gave the corresponding adduct 13j in high yield, albeit with reduced enantioselectivity (entry 10). In addition, 6 promoted the reaction of N-Boc α-aminophenylacetaldehyde (12k) with 11 to yield the corresponding adduct 13k in 68% yield with 60% ee (entry 11).

Table 3. Conjugate additions using organocatalyst 6.

| Entry | Aldehyde | Product | Time (h) | Yield a (%) | ee b (%) |
|-------|----------|---------|----------|-------------|----------|
| 1     | 12a      | 13a     | 2        | 95          | 93       |
| 2     | 12b      | 13b     | 3        | 97          | 89       |
| 3     | 12c      | 13c     | 2        | 95          | 91       |
| 4     | 12d      | 13d     | 2        | 99          | 92       |
| 5     | 12e      | 13e     | 4        | 99          | 92       |
| 6     | 12f      | 13f     | 10       | 98          | 83       |
| 7     | 12g      | 13g     | 4        | 99          | 91       |
| 8     | 12h      | 13h     | 3        | 99          | 92       |
| 9     | 12i      | 13i     | 4        | 97          | 92       |
| 10    | 12j      | 13j     | 77       | 88          | 68       |
| 11    | 12k      | 13k     | 6        | 68          | 60       |

a Isolated yield; b Determined by HPLC analysis.
Based on the optimal conditions for conjugate additions using 6, the reaction conditions were optimized for the enantioselective conjugate additions using 7 (Table 4). 1,2-Dichloroethane was the most suitable solvent among those examined in the presence of 0.1 equiv of TFA at room temperature. The reaction in 1,2-dichloroethane provided high yield and enantioselectivity (entry 8). It should be noted that 7 can promote the conjugate additions in brine because the perfluoroalkyl chain of 7 functions as the hydrophobic reaction field in water as described in our previous report [42,43].

Table 4. Optimization of reaction conditions using organocatalyst 7.

| Entry | Solvent   | Additive (Equiv) | Time (h) | Yield a (%) | ee b (%) |
|-------|-----------|------------------|----------|-------------|----------|
| 1     | toluene   | none             | 24       | 85          | 83       |
| 2     | toluene   | TFA (0.1)        | 2        | 99          | 89       |
| 3     | CH₂Cl₂    | TFA (0.1)        | 2        | 90          | 91       |
| 4     | hexane    | TFA (0.1)        | 2        | 91          | 86       |
| 5     | Et₂O      | TFA (0.1)        | 2        | 85          | 89       |
| 6     | brine     | TFA (0.1)        | 24       | 68          | 78       |
| 7     | CHCl₃     | TFA (0.1)        | 2        | 100         | 91       |
| 8     | ClCH₂CH₂Cl | TFA (0.1)      | 2        | 87          | 92       |
| 9     | m-xylene  | TFA (0.1)        | 2        | 84          | 91       |

a Isolated yield; b Determined by HPLC analysis.

The generality and substrate scope were probed for the optimal conditions (Table 5). The tendency of reactivities using 7 was quite similar to that using 6; however, aldehydes 12e, 12i, and 12j were poor substrates and gave low to moderate yields (entries 5, 9, and 10). Interestingly, the stereoselectivity with 12g was improved up to 94% ee (entry 7). In addition, the yield in the reaction with 12k was improved up to 100% yield (entry 11).

The recyclability of 7 was evaluated. After use of 7 in the conjugate addition of 12a to 11 under the optimal conditions, it was readily recovered by the FSPE technique using fluorous silica gel. Furthermore, the recovered catalyst 7 can be reused without further purification, and its catalytic activity was retained for the first reuse. Unfortunately, the catalytic activity of the recovered catalyst 7 decreased significantly for the second reuse.

We infer that the conjugate additions of aldehydes 12 to vinyl sulfone 11 using 6 or 7 proceed via a plausible transition state (Scheme 3) based on the stereochemistry of addition products 13a–i. The primary amino group of 6 or 7 condenses with aldehydes 12 to generate the corresponding imine intermediate. The imine intermediate is subsequently isomerized to the E-enamine intermediate because of the resonance stabilizing effect of the aromatic ring. Then, the acidic proton of the sulfonamide group, which coordinates intramolecularly to nitrogen in the enamine transition state, successfully interacts with the oxygen of vinyl sulfone to control the approach direction of vinyl sulfone to the Re face of the enamine intermediate. This ultimately affords the corresponding addition
products with high stereoselectivities. We believe that the acidity of 6 and 7 is enhanced by the powerful electron-withdrawing effect of the perfluoroalkyl chains, enabling strong coordination to vinyl sulfone and stabilizing the rigid transition states during conjugate additions. Moreover, the addition of TFA to the conjugate additions might accelerate the formation of the imine and enamine intermediates as well as reinforce the rigid transition state of the conjugate additions.

Table 5. Conjugate additions using organocatalyst 7.

| Entry | Aldehyde | Product | Time (h) | Yield a (%) | ee b (%) |
|-------|----------|---------|----------|-------------|----------|
| 1     | 12a      | 13a     | 2        | 87          | 92       |
| 2     | 12b      | 13b     | 4        | 90          | 90       |
| 3     | 12c      | 13c     | 6        | 100         | 92       |
| 4     | 12d      | 13d     | 2        | 92          | 82       |
| 5     | 12e      | 13e     | 3        | 13          | 80       |
| 6     | 12f      | 13f     | 5        | 100         | 83       |
| 7     | 12g      | 13g     | 4        | 81          | 94       |
| 8     | 12h      | 13h     | 3        | 76          | 92       |
| 9     | 12i      | 13i     | 24       | 45          | 89       |
| 10    | 12j      | 13j     | 24       | 64          | 68       |
| 11    | 12k      | 13k     | 6        | 100         | 64       |

a Isolated yield; b Determined by HPLC analysis.
Scheme 3. Plausible mechanism and transition state model of reaction.

3. Experimental

3.1. General

$^1$H-NMR and $^{13}$C-NMR spectra were measured with a JEOL AL 400 spectrometer (400 MHz for $^1$H-NMR and 100 MHz for $^{13}$C-NMR), or JEOL ECA-500 spectrometer (500 MHz for $^1$H-NMR and 125 MHz for $^{13}$C-NMR). The chemical shifts are expressed in ppm downfield from tetramethylsilane ($\delta = 0.00$) as an internal standard. For thin layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F$_{254}$, Art 5715) were used. The products were isolated by flash column chromatography on silica gel (Kanto Chemical, Tokyo, Japan, silica gel 60N, spherical, neutral, 40–50 μm).

3.2. Preparation of Organocatalyst 6

(S)-tert-Butyl 3-methyl-1-(perfluorobutanesulfonamido)butan-2-ylcarbamate (9). To a solution of (S)-tert-butyl 1-amino-3-methylbutan-2-ylcarbamate (8, 300 mg, 1.48 mmol) [50] in dry CH$_2$Cl$_2$ (5 mL) was added triethylamine (0.46 mL, 3.06 mmol) at room temperature under an argon atmosphere. After stirring for 5 min, perfluorobutanesulfonyl fluoride (0.87 mL, 4.45 mmol) was added to the reaction mixture at 0 °C. After stirring for 1 h at 0 °C, the reaction mixture was additionally stirred for 45 h at room temperature. The reaction mixture was added to water and extracted three times with EtOAc. The EtOAc layers were combined, washed with brine, dried over anhydrous MgSO$_4$, and evaporated. The residue was purified by flash column chromatography on silica gel with a 7:1 mixture of hexane and EtOAc to give the pure 9 (566 mg, 79%) as a colorless powder. Mp = 74–75 °C; $[\alpha]_D^2 = -5.4^\circ$ (c = 0.62 in MeOH); $^1$H-NMR (400 MHz, CD$_3$OD): $\delta = 0.81$ (d, $J = 6.8$ Hz, 3H), 0.85 (d, $J = 6.8$ Hz, 3H), 1.35 (s, 9H), 1.65–1.71 (m, 1H), 3.08 (dd, $J = 8.1, 13.5$ Hz, 1H), 3.28 (dd, $J = 4.5, 13.5$ Hz, 1H), 3.31–3.37 (m, 1H); $^{13}$C-NMR (125 MHz, CD$_3$OD): $\delta = 18.2, 19.9, 28.8, 31.0, 47.1, 57.6, 80.2, 110.2–121.0$ (complex signals of $–$CF$_2$ and $–$CF$_3$), 158.5; HRMS (ESI-TOF): calcd for C$_{14}$H$_{21}$F$_9$N$_2$O$_4$SNa (M+Na)$^+$: 507.0976, Found: 507.0991.

(S)-N-(2-Amino-3-methylbutyl)-perfluorobutanesulfonamide (6). To a solution of 9 (300 mg, 0.619 mmol) in EtOAc (2.5 mL) was added a 4 M solution of hydrochloric acid in EtOAc (2.5 mL) at 0 °C. After stirring for 2.5 h at room temperature, the reaction mixture was evaporated. The residue was added to saturated aqueous NaHCO$_3$ and extracted three times with EtOAc. The EtOAc layers were
combined, washed with brine, dried over anhydrous MgSO₄, and evaporated. The residue was purified by flash column chromatography on silica gel with a 20:1 mixture of CHCl₃ and MeOH to give the pure 6 (214 mg, 90%) as a colorless powder. Mp = 134–136 °C; [α]₀²⁰ = +7.9° (c = 1.01 in MeOH); ¹H-NMR (500 MHz, CD₂OD): δ = 1.01 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H), 1.90–1.97 (m, 1H), 2.82–2.86 (m, 1H), 3.14 (dd, J = 8.6, 13.1 Hz, 1H), 3.41 (dd, J = 3.5, 13.1 Hz, 1H); ¹³C-NMR (125 MHz, CD₂OD): δ = 18.9, 19.0, 30.1, 47.4, 60.7, 110.2–120.4 (complex signals of –CF₂ and –CF₃); Anal. Calcd for C₉H₁₃F₉N₂O₂S: C, 28.13; H, 3.41; N, 7.29. Found: C, 28.07; H, 3.39; N, 7.26.

3.3. Preparation of Organocatalyst 7

(S)-tert-Butyl 3-methyl-1-(perfluorooctanesulfonamido)butan-2-ylcarbamate (10). To a solution of (S)-tert-butyl 1-amino-3-methylbutan-2-ylcarbamate (8) [50] (385 mg, 1.90 mmol) in dry CH₂Cl₂ (20 mL) was added triethylamine (0.80 mL, 5.71 mmol) at room temperature under an argon atmosphere. After stirring for 5 min, perfluorooctane sulfonyl fluoride (1.57 mL, 5.71 mmol) was added to the reaction mixture at 0 °C. After stirring for 2 h at 0 °C, the reaction mixture was additionally stirred for 90 h at room temperature. The reaction mixture was added to water and extracted three times with EtOAc. The EtOAc layers were combined, washed with brine, dried over anhydrous MgSO₄, and evaporated. The residue was purified by flash column chromatography on silica gel with a 6:1 mixture of hexane and EtOAc to give the pure 10 (602 mg, 46%) as a pale yellow oil. [α]₀²⁴ = −4.2° (c = 1.28 in MeOH); ¹H-NMR (500 MHz, CDCl₃): δ = 0.95 (d, J = 7.4 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H), 1.44 (s, 9H), 1.80–1.85 (m, 1H), 3.25 (m, 1H), 3.46 (brd, J = 12.6 Hz, 1H), 3.55 (m, 1H), 4.67 (brd, J = 8.0 Hz, 1H), 7.13 (brs, 1H); ¹³C-NMR (125 MHz, CDCl₃): δ = 18.0, 19.2, 28.2, 30.1, 48.4, 55.7, 80.8, 108.0–113.0 (complex signals of –CF₂ and –CF₃), 157.6; HRMS (ESI-TOF): calcd for C₁₈H₂₁F₁₇N₂O₄SNa (M+Na)+: 707.0848, Found: 707.0873.

(S)-N-(2-Amino-3-methylbutyl)-perfluorooctanesulfonamide (7). To a solution of 10 (570 mg, 0.833 mmol) in EtOAc (3.5 mL) was added a 4M solution of hydrochloric acid in EtOAc (3.5 mL) at 0 °C. After stirring for 2 h at room temperature, the reaction mixture was evaporated. The residue was added to saturated aqueous NaHCO₃ and extracted three times with EtOAc. The EtOAc layers were combined, washed with brine, dried over anhydrous MgSO₄, and evaporated. The residue was purified by flash column chromatography on silica gel with a 20:1 mixture of CHCl₃ and MeOH to give the pure 7 (444 mg, 91%) as a colorless powder. Mp = 144–145 °C; [α]₀²⁴ = +6.9° (c = 1.01 in MeOH); ¹H-NMR (500 MHz, CD₂OD): δ = 1.01 (d, J = 6.8 Hz, 3H), 1.03 (d, J = 6.8 Hz, 3H), 1.90–1.97 (m, 1H), 2.82–2.86 (m, 1H), 3.15 (dd, J = 8.5, 13.1 Hz, 1H), 3.41 (dd, J = 4.0, 13.1 Hz, 1H); ¹³C-NMR (125 MHz, CD₂OD): δ = 18.9, 19.0, 30.1, 47.5, 60.7, 109.7–121.5 (complex signals of –CF₂ and –CF₃); Anal. Calcd for C₁₃H₁₃F₁₇N₂O₄S: C, 26.72; H, 2.24; N, 4.79. Found: C, 26.75; H, 2.41; N, 4.86.

3.4. Typical Procedure for Michael Addition (Table 3)

A typical procedure of the Michael additions using 6 is as follows: To a solution of 11 (30.8 mg, 0.100 mmol) and organocatalyst 6 (3.8 mg, 0.010 mmol) in m-xylene (1.0 mL) was added 2-phenylpropanal (26.8 µL, 0.200 mmol) and trifluororacetic acid (0.7 µL, 0.010 mmol) at room temperature. After stirring at room temperature for 2 h, the reaction mixture was directly purified by
flash column chromatography on silica gel with a 3:1 mixture of hexane and EtOAc to afford the pure 13a (42.0 mg, 95%) as a colorless powder. All the Michael addition products 13 in the paper are known compounds that exhibited spectroscopic data identical to those reported in the literature [36,37].

(R)-2-Methyl-2-phenyl-4,4-bis(phenylsulfonyl)butanal (13a). [α]D 18 = −25.6° (c = 1.00, CHCl3); 95% ee; enantiomeric excess was determined by HPLC with Chiralpak AS-H column (hexane/2-propanol = 70:30), flow rate = 1.0 mL/min; λ = 220 nm; tmajor = 21.7 min, tminor = 25.9 min.

(R)-2-(4-Bromophenyl)-2-methyl-4,4-bis(phenylsulfonyl)butanal (13b). [α]D 22 = −15.2° (c = 1.00, CHCl3); 89% ee; enantiomeric excess was determined by HPLC with Chiralpak AS-H column (hexane/2-propanol = 70:30), flow rate = 1.0 mL/min; λ = 220 nm; tmajor = 27.1 min, tminor = 38.5 min.

(R)-2-(4-Fluorophenyl)-2-methyl-4,4-bis(phenylsulfonyl)butanal (13c). [α]D 18 = +23.5° (c = 1.00, CHCl3); 91% ee; enantiomeric excess was determined by HPLC with Chiralpak AS-H column (hexane/2-propanol = 70:30), flow rate = 1.0 mL/min; λ = 220 nm; tmajor = 25.5 min, tminor = 32.1 min.

(R)-2-Methyl-2-(naphthalen-2-yl)-4,4-bis(phenylsulfonyl)butanal (13h). [α]D 18 = +13.0° (c = 1.00, CHCl3); 92% ee; enantiomeric excess was determined by HPLC with Chiralpak AS-H column (hexane/2-propanol = 70:30), flow rate = 1.0 mL/min; λ = 220 nm; tmajor = 32.9 min, tminor = 39.1 min.

(R)-2-Methoxy-2-phenyl-4,4-bis(phenylsulfonyl)butanal (13j). 68% ee; enantiomeric excess was determined by HPLC with Chiralcel AD-H column (hexane/2-propanol = 5:1), flow rate = 1.0 mL/min; λ = 220 nm; tmajor = 37.1 min, tminor = 44.5 min.
(R)-tert-Butyl 1-oxo-2-phenyl-4,4-bis(phenylsulfonyl)butan-2-ylcarbamate (13k). $[\alpha]_{D}^{25} = +10.0^\circ$ (c = 1.00, CHCl$_3$) 64% ee; enantiomeric excess was determined by HPLC with Chiralcel OD-H column (hexane/2-propanol = 90:10), flow rate = 0.5 mL/min; $\lambda = 220$ nm; $t_{\text{major}} = 19.9$ min, $t_{\text{minor}} = 22.2$ min.

4. Conclusions

Novel organocatalysts 6 and 7 can easily be prepared from L-valine, an inexpensive and commercially available natural amino acid. Organocatalysts 6 and 7, which are simple $\beta$-aminosulfonamides with only one stereogenic center, efficiently catalyze the conjugate additions of various branched aldehydes to vinyl sulfone 11 with a short reaction time at room temperature to give the corresponding addition products possessing all-carbon quaternary stereocenters with high enantioselectivities. The excellent performance is probably due to the carbon skeleton of L-valine and the electron-withdrawing effect of the perfluoroalkyl groups on 6 and 7. Moreover, fluorous organocatalyst 7 bearing a perfluorooctyl group was readily recovered by simple solid phase extraction using fluorous silica gel and was immediately reusable without further purification for the first cycle. Further application of these organocatalysts in the synthesis of bioactive compounds is currently being investigated in our laboratory.

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Conflicts of Interest

The authors declare no conflict of interest.

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