JOC The Journal of Organic Chemistry

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Organocatalytic Tandem Three-Component Reaction of Imine, Alkyl Vinyl Ketone, and Imide via aza-Baylis−Hillman Reaction

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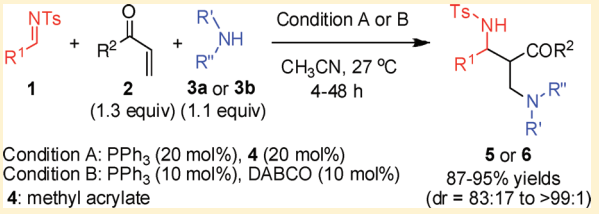
Supporting Information

ABSTRACT: A highly chemoselective PPh_3-catalyzed three-component reaction of an imine, alkyl vinyl ketone, and phthalimide or succinimide is developed. Various highly functional adducts with high diastereoselectivities can be generated via aza-Morita−Baylis−Hillman reactions of aryl-substituted imines and alkyl vinyl ketones followed by Michael additions of imides and then epimerization.

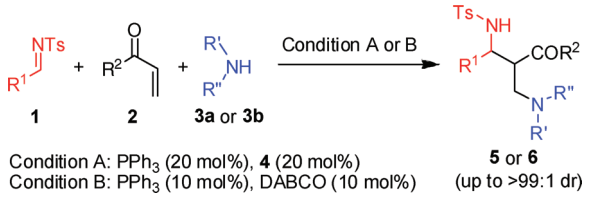


Multicomponent reactions are of great importance in organic synthesis due to generation of an adduct in a single operation from three or more reactants with high atom economy and bond-forming efficiency.[1] In addition, good chemoselectivities in the presence of all the reactants make the multicomponent reaction a useful methodology to construct complex molecules.[2] The aza-Baylis−Hillman adducts,[3] starting from imines and alkyl vinyl ketones, are excellent Michael acceptors due to the ketone functionality activated by the neighboring sulfonimide group via hydrogen bonding interaction. Their application in the Michael addition reactions with nucleophiles can further provide various highly functional products.[3,4]

Recently, we reported an $EtPPh_2$- or PPh_3-catalyzed tandem three-component reaction of aldehyde, alkyl acrylate (or alkyl vinyl ketone), and amide.[5] Since the aza-Baylis−Hillman adducts are better Michael acceptors than alkyl vinyl ketones, it should be possible to conduct a phosphine-catalyzed three-component reaction starting from the aza-Baylis−Hillman reaction of imine **1** and alkyl vinyl ketone **2**, followed by the Michael addition of imide **3** to the resulting adduct. Herein, we wish to report a highly diastereoselective and chemoselective three-component reaction of **1**, **2**, and **3** catalyzed by PPh_3 and methyl acrylate (**4**) or 1,4-diazabicyclo[2.2.2]octane (DABCO), affording the adducts **5** and **6** (Scheme 1).

The imine **1a**, methyl vinyl ketone (**2a**) (1.5 equiv), and phthalimide (**3a**) (1.1 equiv) in the presence of PPh_3 (20 mol %) in tetrahydrofuran (THF) reacted successfully at 27 °C within 7 h ($t1$, full conversion of **1a**), providing the highly functional three-component adduct **5a** in high isolated yield (96%), albeit with poor diastereoselectivity (54:46) (entry 1, Table 1). In order to improve the diastereoselectivity of **5a**, several additives such as DABCO, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), or **4** were evaluated (Figure 1). The additive **4** was chosen because the *in situ* formed enolate **10**, which resulted from the Michael addition of PPh_3 to **4**, could be an effective base.[6] In addition, different solvents were examined (entries 2−10). DABCO (20 mol %) catalyzed the aza-Baylis−Hillman reaction of **1a** and **2a**,

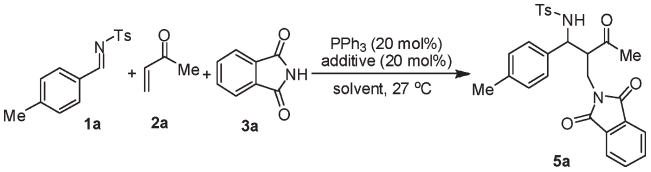
Scheme 1. Tandem Three-Component Reaction of Imine 1, Alkyl Vinyl Ketone 2, and Imide 3



giving the corresponding adduct **5a** more efficiently ($t1$ = 2 h) with improved diastereoselectivity (74:26, entry 2). Interestingly, with slightly less **2a** (1.3 equiv), the dr of **5a** increased slightly ($t1$ = 2 h; 75%; 80:20 dr; entry 3). When DABCO (40 mol %) was used without PPh_3, it took longer ($t1$ = 12 h) to furnish **5a** (85% yield; 75:25 dr) (entry 4). Furthermore, we found a slightly increased dr of **5a** (80:20) after 48 h ($t2$) under the same reaction conditions. Different solvents, such as CH_2Cl_2, dimethylformamide (DMF), or CH_3CN, were screened when both PPh_3 (20 mol %) and DABCO (20 mol %) were used, and CH_3CN turned out to be the best one for the formation of **5a** (0.5 h; 95% isolated yield) (entries 5−7). Even reduced PPh_3 (10 mol %) and DABCO (10 mol %) can efficiently catalyze the reaction of **1a**, **2a** (1.3 equiv), and **3a** (1.1 equiv), affording **5a** within 0.5 h (100% yield; 50:50 dr) (entry 8). DBU (20 mol %) gave an inferior result to that of DABCO (entries 7 and 9). Surprisingly, in the presence of methyl acrylate (**4**) (20 mol %) and PPh_3 (20 mol %), the reaction of **1a**, **2a** (1.3 equiv), and **3a** (1.1 equiv) in CH_3CN took place effectively within 0.5 h, providing **5a** in 95% isolated yield with 45:55 dr, and the diastereoselectivity of **5a** was up to 88:12 after 48 h (entry 10).[7]

Received: October 28, 2010
Published: March 14, 2011

Table 1. Optimization of Reaction Conditions for an Organocatalytic Three-Component Reaction of 1a, 2a, and 3a[a]



entry	additive	solvent	*t*1; *t*2 (h)	NMR yield of **5a** (*t*1) (%)[b]; dr (*t*1; *t*2)[c]
1[d]	none	THF	7; 48	96[e]; (54:46; 54:46)
2[d]	DABCO	THF	2; 48	95; (74:26; 75:25)
3	DABCO	THF	2; 48	75; (80:20; 80:20)
4[f]	DABCO	THF	12; 48	85; (75:25; 80:20)
5	DABCO	CH_2Cl_2	2; 48	90; (66:34; 80:20)
6	DABCO	DMF	1; 48	85[e]; (50:50; 50:50)
7	DABCO	CH_3CN	0.5; 48	100[g]; (60:40; 75:25)
8[h]	DABCO	CH_3CN	0.5; 48	100; (50:50; 75:25)
9	DBU	CH_3CN	0.5; 48	80; (50:50; 73:27)
10	**4**	CH_3CN	0.5; 48	100[g]; (45:55; 88:12)

[a] Reactions were carried out using **1a** (1.0 mmol), **2a** (1.3 equiv), and **3a** (1.1 equiv) in solvent (1.0 mL) at 27 °C. [b] DMF was used as the internal standard. [c] Diastereoselectivities (*erythro*/*threo*) of **5a** at *t*1 and *t*2 were determined by crude ^{1}H NMR analysis. [d] 1.5 equiv of **2a** was used. [e] Isolated yield. [f] The reaction proceeded only with DABCO (40 mol %). [g] 95% isolated yield. [h] PPh_3 (10 mol %) and DABCO (10 mol %) were used.

The broad reaction scope of our optimized protocol was demonstrated in Table 2 (condition A, PPh_3 (20 mol %) and **4** (20 mol %); condition B, PPh_3 (10 mol %) and DABCO (10 mol %)). It showed that, under condition A, highly chemoselective three-component reactions of various aryl-substituted imines such as **1a**−**1b**, **1d**−**1f**, **1g**, or **1i**−**1j**, **2a** or **2b** (1.3 equiv), and **3a** (1.1 equiv) completed in 0.5−1 h, leading to the corresponding adducts **5a**−**5b**, **5d**, **5g**, **5i**−**5j**, or **5n**, **5o** with poor to moderate diastereoselectivities (50:50 to 30:70), except for **5e** (8:92 dr).[8] When the reactions proceeded with prolonged time (3−48 h), high diastereoselectivities of **5a**−**5b**, **5d**−**5e**, **5g**, **5i**−**5j** or **5n**−**5o** were obtained (**5a**, **5i**−**5k**, 90:10 to 83:17 dr; **5b**, **5d**−**5e**, **5g**, **5n**−**5o**, 17:83 to 2:98 dr) (entries 1−2, 4−5, 7, 9−10, and 14−15). The reactions of **1c**, **1f**, or **1h**, **2a** (1.3 equiv) and **3a** (1.1 equiv), which gave unsatisfactory results under condition A, were carried out in the presence of PPh_3 (10 mol %) and DABCO (10 mol %) within 8−48 h with good results (**5c**, 92%, 87:13 dr; **5f**, 90%, 9:91 dr; **5h**, 91%, 15:85 dr) (entries 3, 6, and 8). A heteroaryl-subsitituted imine, such as **1k** or an imine **1l**, reacted successfully with **2a** and **3a** according to our protocol (**1k**, condition A; **1l**, condition B), affording the corresponding adduct **5k** or **5l** in high yields and with good diastereoselectivities (**5k**, 87%, 88:12 dr; **5l**, 87%, 5:95 dr) (entries 11 and 12). An alkyl-substituted imine like **1m** was examined; however, no reaction of **1m**, **2a**, and **3a** occurred (entry 13).

Furthermore, a different imide, such as succinimide (**3b**) (1.1 equiv), also worked nicely with an aryl-substituted imine like **1b**, **1c**, **1e**, or **1g** (R = 4-$CH_3OC_6H_4$, C_6H_5, 4-$NO_2C_6H_4$, 4-BrC_6H_4) and **2a** (1.3 equiv) in the presence of PPh_3 (20 mol %) and **4** (20 mol %) within 3−36 h, providing **6a**−**6d** with high to excellent diastereoselectivities (13:87 to <1:99) (entries 1−4, Table 3).[8]

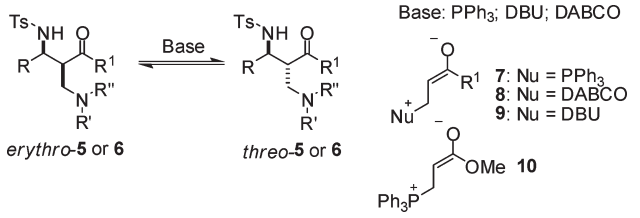
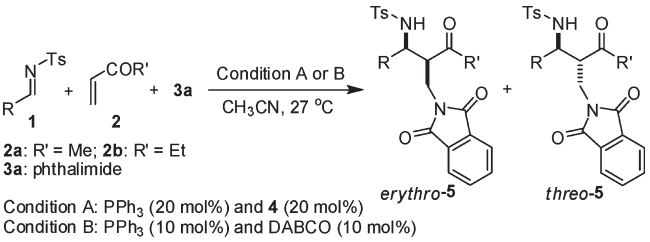


Figure 1. Possible bases in our designed condition for deprotonation of the α-position of ketone function of **5** or **6** facilitating the change of the ratio of two diastereomers of **5** or **6**.

Table 2. Three-Component Reaction of Imine 1, 2, and 3a[a]



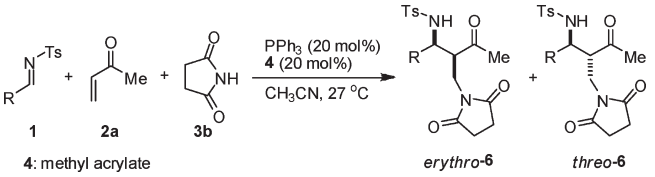
entry	R; R′	time (h)	yield (%)[b]; dr[c]
1[d]	4-$CH_3C_6H_4$; Me	48	**5a**, 95; 88:12
2[d]	4-$CH_3OC_6H_4$; Me	24	**5b**, 90; 2:98
3[e]	C_6H_5; Me	48	**5c**, 92; 83:17[f]
4[d]	2-naphthyl; Me	48	**5d**, 93; 2:98[f]
5[d]	4-$NO_2C_6H_4$; Me	4	**5e**, 93; 6:94[f]
6[e]	4-$CF_3C_6H_4$; Me	8	**5f**, 90; 9:91
7[d]	4-BrC_6H_4; Me	48	**5g**, 95; 3:97[f]
8[e]	4-ClC_6H_4; Me	8	**5h**, 91; 15:85
9[d]	2-BrC_6H_4; Me	48	**5i**, 85; 90:10[f]
10[d]	2-ClC_6H_4; Me	48	**5j**, 90; 90:10
11[d]	2-thienyl; Me	24	**5k**, 87; 88:12[g]
12[e]	*trans*-PhCH=CH; Me	24	**5l**, 87; 5:95[g]
13[d]	*i*-Pr; Me		**5m**, no reaction
14[d]	4-BrC_6H_4; Et	12	**5n**, 87; 4:96
15[d]	4-$CF_3C_6H_4$; Et	3	**5o**, 95; 17:83

[a] Reactions were carried out using **1** (1.0 mmol), **2** (1.3 equiv), and **3a** (1.1 equiv) in CH_3CN (1.0 mL) at 27 °C. [b] Yield of isolated product. [c] Diastereoselectivities (*erythro*/*threo*) of **5** were determined by crude ^{1}H NMR analysis; the stereochemistry of **5** was determined by ^{1}H NMR analysis in comparison to **5e**, **5g**, and **5i**. [d] Condition A. [e] Condition B. [f] The relative configuration was confirmed by X-ray crystallography. [g] The relative configuration was not determined.

On the basis of experimental results (Tables 1−3), a plausible reaction mechanism for this highly chemoselective three-component reaction was proposed (Scheme 2).[9,10] First, a PPh_3-catalyzed aza-Baylis−Hillman reaction took place, giving rise to the corresponding adduct **11**. Deprotonation of an imide **3** occurred, and **12** underwent the Michael addition toward **11** followed by protonation, affording the corresponding adduct **5** or **6** with the regeneration of PPh_3. The different solubilities of *erythro*-**5** and *threo*-**5** (or *erythro*-**6** and *threo*-**6**) in CH_3CN probably accounted for the diastereoselectivities of **5** (or **6**). The base, such as DABCO or an *in situ* formed base resulting from the addition of PPh_3 toward **4**, deprotonated the α-position

dx.doi.org/10.1021/jo102143r |*J. Org. Chem.* 2011, 76, 2888–2891

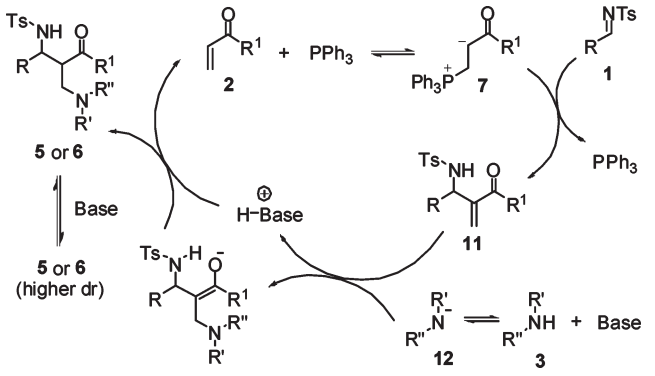
Table 3. Three-Component Reaction of Imines 1, 2a, and 3b[a]



entry	R	time (h)	yield (%)[b]; dr[c]
1	4-$CH_3OC_6H_4$	36	**6a**, 88; 13:87
2	C_6H_5	36	**6b**, 93; 9:91
3	4-$NO_2C_6H_4$	3	**6c**, 94; <1:99
4	4-BrC_6H_4	12	**6d**, 91; 5:95

[a] Reactions were carried out using **1** (1.0 mmol), **2a** (1.3 equiv), and **3b** (1.1 equiv) in CH_3CN (1.0 mL) at 27 °C. [b] Yield of isolated product. [c] Diastereoselectivities (*erythro*/*threo*) of **6** were determined by crude ^{1}H NMR analysis; the relative configuration of **6a**−**6d** was confirmed by X-ray crystallography.

Scheme 2. Proposed Mechanism of the Three-Component Reaction of 1, 2, and 3 Catalyzed by PPh_3



of ketone function of **5** or **6** and facilitated the change of the ratio of the two diastereomers of **5** or **6**.

In summary, we have developed a general procedure for the highly diastereoselective and chemoselective three-component reaction of imine **1**, alkyl vinyl ketone **2**, and imide **3** catalyzed by PPh_3 and DABCO or methyl acrylate (**4**). The reaction conditions are very mild, and numerous aryl-substituted imines **1** can react efficiently with **2** and **3** in high yields. The reaction mechanism is proposed to undergo the aza-Morita−Baylis−Hillman reaction of **1** and **2** followed by the Michael addition of **12** toward the corresponding adduct **11**. Our study indicated that in combination with PPh_3, **4** can improve the diastereoselectivities of **5** or **6** when two diastereomers of **5** or **6** have different solubilities in CH_3CN. Further studies and the extensions of this work in other activated alkenes, as well as the use of other nucleophilic reagents, are currently underway.

EXPERIMENTAL PROCEDURE

General Procedure. *Preparation of N-[2-Acetyl-1-(4-methylphenyl)-3-phthalimidopropyl]-p-toluenesulfonamide* ***5a****:* A dry and nitrogen-flushed 10 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with a solution of **1a** (273.1 mg, 1.0 mmol), **3a** (161.7 mg, 1.1 equiv), and PPh_3 (52.4 mg, 20 mol %) in dry CH_3CN (1.0 mL). Methyl vinyl ketone (**2a**) (105.4 μL, 1.3 equiv) and methyl acrylate (**4**) (18.0 μL, 20 mol %) were added, and the reaction mixture was stirred for 48 h at 27 °C. Thereafter, the solvent was removed by evaporation in vacuo. Purification by flash chromatography (CH_2Cl_2/CH_3OH 100:1) furnished the adducts *erythro*-**5a** and *threo*-**5a** as a white solid (419.0 mg) and a white solid (46.7 mg), respectively (overall 95% yield).

erythro-***5a****:* R_f 0.19 (CH_2Cl_2/CH_3OH, 120/1); mp, 171.2−171.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm, 7.76−7.68 (m, 2H), 7.68−7.61 (m, 2H), 7.55 (d, 2H, J = 8.0 Hz), 7.10 (d, 2H, J = 8.0 Hz), 6.86 (d, 2H, J = 7.8 Hz), 6.77 (d, 2H, J = 7.8 Hz), 5.86 (d, 1H, J = 9.2 Hz), 4.73 (pseudo t, 1H, J = 8.4 Hz), 4.11 (dd, 1H, J = 14.6, 6.4 Hz), 4.0 (dd, 1H, J = 14.6, 7.6 Hz), 3.65−3.54 (m, 1H), 2.33 (s, 3H), 2.06 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ/ppm, 207.2, 168.0, 142.9, 137.5, 137.2, 134.4, 133.9, 131.6, 129.1, 128.9, 127.0, 126.4, 123.1, 57.1, 56.1, 36.7, 30.0, 21.3, 20.7; MS (20 eV, EI) m/z (%), 335 [M − 154]$^+$ (10), 273 (100), 217 (70), 174 (89), 155 (68), 118 (96), 92 (16); IR (CH_2Cl_2) ν (cm^{-1}), 3210 (s), 2922 (m), 1775 (s), 1723 (s), 1325 (m), 1155 (m), 938 (m), 717 (s); HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2O_5SNa$, [M + Na]$^+$ (513.1460), found, 513.1458. Anal. Calcd. for $C_{27}H_{26}N_2O_5S$: C, 66.10; H, 5.34; N, 5.71; S, 6.54. Found: C, 65.88; H, 5.31; N, 6.04; S, 6.67.

threo-***5a****:* R_f 0.15 (CH_2Cl_2/CH_3OH, 120/1); mp, 172.1−172.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm, 7.85−7.72 (m, 2H), 7.72−7.60 (m, 2H), 7.40 (d, 2H, J = 8.0 Hz), 6.97 (d, 2H, J = 8.0 Hz), 6.89 (d, 2H, J = 7.8 Hz), 6.83 (d, 2H, J = 7.8 Hz), 6.20 (d, 1H, J = 9.7 Hz), 4.68 (pseudo t, 1H, J = 8.6 Hz), 4.00−3.86 (m, 1H), 3.61−3.47 (m, 2H), 2.26 (s, 3H), 2.16 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ/ppm, 209.6, 167.8, 142.7, 137.6, 137.4, 134.5, 134.1, 131.6, 129.1, 129.0, 126.9, 126.5, 123.3, 58.1, 55.7, 37.8, 30.7, 21.3, 20.8; MS (20 eV, EI) m/z (%), 336 [M − 154]$^+$ (100), 275 (80), 218 (25), 188 (28), 155 (18), 118 (30), 92 (7); IR (CH_2Cl_2) ν (cm^{-1}), 3210 (s), 2922 (m), 1775 (s), 1723 (s), 1325 (m), 1155 (m), 938 (m), 717 (s); HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2O_5SNa$, [M + Na]$^+$ (513.1460); found, 513.1464.

Preparation of N-[2-Acetyl-1-(4-trifluoromethyl-phenyl)-3-phthalimidopropyl]-p-toluenesulfonamide ***5f****:* A dry and nitrogen-flushed 10 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was charged with a solution of **1f** (327.0 mg, 1.0 mmol), **3a** (161.7 mg, 1.1 equiv), PPh_3 (26.2 mg, 10 mol %), and DABCO (11.2 mg, 10 mol %) in dry CH_3CN (1.0 mL). Methyl vinyl ketone (**2a**) (105.4 μL, 1.3 equiv) was added, and the reaction mixture was stirred for 8 h at 27 °C. Thereafter, the solvent was removed by evaporation in vacuo. Purification by flash chromatography (CH_2Cl_2/CH_3OH 100:1) furnished the adducts *erythro*-**5f** and *threo*-**5f** as a white solid and a white solid, respectively (*erythro*-**5f**, 33.5 mg; *threo*-**5f**, 439.6 mg; mixture of **5f**, 16.6 mg; overall 489.7 mg, 90%).

erythro-***5f****:* R_f 0.19 (CH_2Cl_2/CH_3OH, 120/1); mp, 179.1−180.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm, 7.71−7.65 (m, 4H), 7.53 (d, 2H, J = 8.0 Hz), 7.19 (d, 2H, J = 8.3 Hz), 7.15 (d, 2H, J = 8.3 Hz), 7.10 (d, 2H, J = 8.0 Hz), 6.05 (d, 1H, J = 9.0 Hz), 4.93 (pseudo t, 1H, J = 7.8 Hz), 4.11 (dd, 1H, J = 14.8, 7.2 Hz), 3.99 (dd, 1H, J = 14.8, 7.2 Hz), 3.67−3.62 (m, 1H), 2.33 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ/ppm, 206.0, 168.2, 143.6, 141.6, 137.4, 134.3, 131.4, 129.8 (J = 32.0 Hz), 129.4, 127.1, 126.9, 125.2 (J = 3.0 Hz), 123.5 (J = 271.0 Hz), 123.3, 56.3, 55.4, 35.7, 29.9, 21.3; MS (20 eV, EI) m/z (%), 389 [M − 155]$^+$ (98), 328 (52), 242 (100), 217 (75), 174 (22), 155 (74), 147 (10); IR (KBr) ν (cm^{-1}), 3276 (s), 3070 (w), 2929 (w), 1775 (s), 1719 (s), 1329 (s), 1170 (s), 894 (m), 676 (m), 565 (m); HRMS (ESI) m/z calcd for $C_{27}H_{23}F_3N_2O_5SNa$ [M + Na]$^+$ 567.1177; found, 567.1169.

threo-***5f****:* R_f 0.14 (CH_2Cl_2/CH_3OH, 120/1); mp, 187.9−189.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm, 7.83 (dd, 2H, J = 5.3, 3.0 Hz), 7.72

dx.doi.org/10.1021/jo102143r |*J. Org. Chem.* 2011, 76, 2888–2891

(dd, 2H, J = 5.3, 3.0 Hz), 7.39 (d, 2H, J = 8.0 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.10 (d, 2H, J = 8.0 Hz), 6.97 (d, 2H, J = 8.0 Hz), 6.27 (d, 1H, J = 9.6 Hz), 4.81 (dd, 1H, J = 9.6, 6.4 Hz), 4.00 (dd, 1H, J = 14.2, 8.4 Hz), 3.64 (dd, 1H, J = 14.2, 5.5 Hz), 3.58−3.55 (m, 1H), 2.33 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ/ppm, 2209.5, 167.8, 143.3, 141.8, 137.5, 134.3, 131.6, 129.9 (J = 32.0 Hz), 129.2, 127.2, 126.9, 125.4 (J = 3.0 Hz), 123.7 (J = 270.0 Hz), 123.6, 57.8, 55.2, 37.9, 31.4, 21.2; MS (20 eV, EI) m/z (%), 389 $[M - 155]^+$ (100), 328 (32), 242 (67), 217 (48), 174 (36), 155 (93); IR (KBr) ν (cm^{-1}), 3276 (s), 3070 (w), 2929 (w), 1775 (s), 1719 (s), 1329 (s), 1170 (s), 894 (m), 676 (m), 565 (m); HRMS (ESI) m/z calcd for $C_{27}H_{24}F_3N_2O_5S$ $[M + H]^+$ 545.1358; found, 545.1364.

■ ASSOCIATED CONTENT

Supporting Information. General experimental procedures, compound characterization data, X-ray crystallographic data (CCDC numbers *threo*-**5c** (785230), *threo*-**5d** (785231), *threo*-**5e** (748322), *threo*-**5g** (785232), *threo*-**5i** (785233), *threo*-**6a** (785234), *threo*-**6b** (785235), *threo*-**6c** (785236), and *threo*-**6d** (785237)), and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

We thank the National Science Council of the Republic of China (NSC Grant No. 99-2113-M-003-004-MY2) and National Taiwan Normal University (Grant 99T3030-6) for financial support.

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(7) The different solubilities of *erythro*-**5** and *threo*-**5** (or *erythro*-**6** and *threo*-**6**) in CH_3CN probably accounted for the diastereoselectivities of **5** (or **6**). We found that the solubilities of **5** or **6** were not good, and all of **5** or **6** precipitated during the reaction progress. The dr of **5** or **6** was determined by crude ^{1}H NMR analysis when all the products were well dissolved in solution by adding excess of the corresponding solvent (Tables 1−3). The base, such as DABCO or an *in situ* formed base **10**, accelerated the change of the ratio of two diastereomers of **5** or **6** in the solution.

(8) For more details, please see the Supporting Information.

(9) Because PPh_3 was a better catalyst than DABCO in our designed three-component reaction and the corresponding aza-Baylis−Hillman reaction (Table 1), PPh_3 was used as the representive catalyst for the reaction of **1**, **2**, and **3** in the proposed reaction mechanism, and even DABCO can also catalyze this process.

(10) In order to elucidate how DABCO influences the change of dr of **5**, two controlled experiments of *erythro*-**5f** or *threo*-**5f** with CD_3OD in the presence of DABCO in $CDCl_3$ were carried out. It was found that DABCO smoothly deprotonated the α-position of the ketone function of both *erythro*-**5f** and *threo*-**5f**. For mechanism studies, please see the Supporting Information.