Synthetic Methods

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Catalytic Enantioselective Michael Addition of 1-Fluoro-bis(phenylsulfonyl)methane to α,β-Unsaturated Ketones Catalyzed by Cinchona Alkaloids**

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There is a high demand in both academia and industry for enantiopure fluorine-containing organic molecules because of their unique pharmacological properties.[1] Although their occurrence in natural systems is rare,[2] monofluorinated analogues of biologically active compounds are often evaluated as bioisosteres of the parent molecules.[1,3] Compounds with monofluoromethyl groups are also important in biological systems.[4] The current state-of-the-art asymmetric catalysis uses organocatalysts or ligand–metal complexes that allow access to the chiral monofluorinated organic compounds with high enantiocontrol.[5] However, most of the recent innovations in this area are based on the enantioselective fluorination reactions developed by us and others.[5,6] In comparison, the enantioselective fluoromethylation reactions still need to be investigated.[7] In 2006, we disclosed 1-fluorobis(phenylsulfonyl)methane (FBSM) as a synthetic equivalent of a monofluoromethide species under the palladium-catalyzed Tsuji–Trost allylic alkylation conditions, which provided the first asymmetric allylic monofluoromethylation with high enantiocontrol.[8a] Hu and co-workers, and Prakash, Olah, and co-workers demonstrated the effectiveness of FBSM for achieving monofluoromethylation in the non-asymmetric epoxide ring-opening and Mitsunobu reactions.[9] Recently, we reported the FBSM-based catalytic enantioselective Mannich-type monofluoromethylation which provided chiral α-fluoromethylamines with excellent enantioselectivities.[8b] On the basis of this concept we used FBSM as a potential monofluoromethide equivalent, and report herein the first catalytic, asymmetric 1,4-conjugate addition of FBSM to α,β-unsaturated ketones. The ammonium salts of cinchona alkaloids possessing sterically demanding substituents effectively catalyzed the conjugate addition reaction to furnish Michael adducts in high yield with excellent enantioselectivity.

The catalytic asymmetric Michael addition reaction is one of the most powerful tools for carbon–carbon bond-forming reactions.[10] Either chiral quaternary ammonium salts or chiral Lewis acids can be successfully used as catalysts for achieving high enantiocontrol. There are many reports of the catalytic asymmetric conjugate addition of nucleophiles to a Michael acceptor; however, it has not been extended to asymmetric fluoromethylations.[11,15] On the basis of our work on asymmetric monofluoromethylations, FBSM was envisioned to function as a Michael-type donor under suitable conditions. This assumption was first tested on the reaction of FBSM with chalcone (**1a**) under our best conditions for asymmetric Mannich-type fluoromethylation,[8b] which employed benzylquinidinium chloride (QD-**3a**; X = Cl) as a catalyst (10 mol%) in the presence excess $CsOH{\cdot}H_2O$ (3.0 equiv) in CH_2Cl_2 at low temperature. The initial results were quite discouraging as the reaction produced Michael adduct **2a** in a 62% yield with a low *ee* value (Table 1, entry 1). The *ee* value was improved to 44% when the reaction was performed in the presence of K_2CO_3 (Table 1, entry 2). After screening various bases and solvents (Table 1, entries 3–8), a catalytic amount of QD-**3a** (X = Cl) and 3 equivalents of Cs_2CO_3 in CH_2Cl_2 provided (*S*)-**2a** with the highest enantioselectivity (Table 1, entry 4). Attempts to improve the enantioselectivity of the product by using catalyst QD-**4** failed, providing **2a** in a low yield with 27% *ee* (Table 1, entry 9). This finding indicated that the free hydroxy group of the cinchona alkaloid is indispensable for achieving high enantiocontrol. Ammonium salts, CN-**3a** and CD-**3a**, derived from cinchonine and cinchonidine, respectively, were less effective (Table 1, entries 11 and 12). An extensive screening of cinchona alkaloids was performed under the same conditions (Table 1, entries 10–17), and we found that the quinidinium chloride (QD-**3f**; X = Br), bearing a sterically demanding benzyl substituent, was effective at providing **2a** in high yield with an excellent *ee* value of 97% (Table 1, entry 17). We also discovered that by using the analogous ammonium bromide derived from quinine (QN-**3f**; X = Br), a similar enantioselectivity was obtained for **2a**, albeit with the opposite (*R*) stereochemistry (Table 1, entry 18).[12] Notably, for the reaction of **1a** with FBSM at low catalyst loading (5 mol%), the same high *ee* value of (*S*)-**2a** was obtained (Table 1, entry 19).

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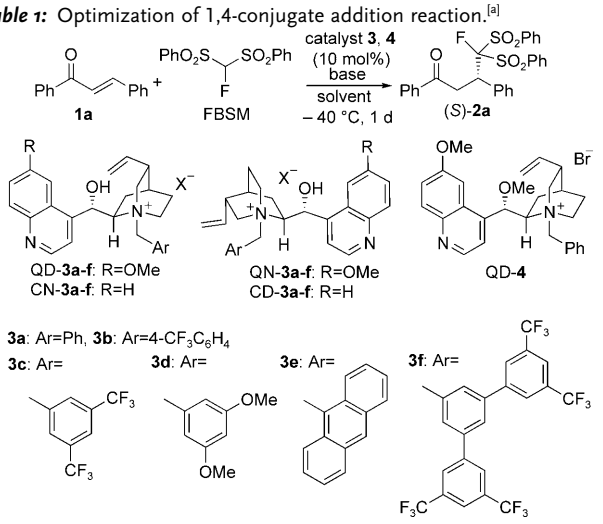
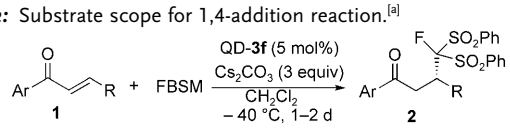
Table 1: Optimization of 1,4-conjugate addition reaction.[a]



Entry	Cat.	Base	Solvent	Yield[b] [%]	*ee* [%]
1	QD-**3a**[c]	$CsOH·H_2O$	CH_2Cl_2	62	8
2	QD-**3a**[c]	K_2CO_3	CH_2Cl_2	81	44
3	QD-**3a**[c]	K_2CO_3[e]	CH_2Cl_2	81	44
4	QD-**3a**[c]	Cs_2CO_3	CH_2Cl_2	82	72
5	QD-**3a**[c]	Cs_2CO_3	toluene	53	41
6	QD-**3a**[c]	Cs_2CO_3	CH_2Cl_2/toluene (7:3)	58	55
7	QD-**3a**[c]	Cs_2CO_3	THF	52	36
8	QD-**3a**[c]	Cs_2CO_3	*t*BuOMe	2	28
9	QD-**4**	Cs_2CO_3	CH_2Cl_2	21	27
10	QN-**3a**[c]	Cs_2CO_3	CH_2Cl_2	73	62[f]
11	CN-**3a**[c]	Cs_2CO_3	CH_2Cl_2	33	57
12	CD-**3a**[c]	Cs_2CO_3	CH_2Cl_2	54	37[f]
13	QD-**3b**[d]	Cs_2CO_3	CH_2Cl_2	60	60
14	QD-**3c**[d]	Cs_2CO_3	CH_2Cl_2	59	67
15	QD-**3d**[c]	Cs_2CO_3	CH_2Cl_2	67	34
16	QD-**3e**[d]	Cs_2CO_3	CH_2Cl_2	50	21[f]
17	QD-**3f**[d]	Cs_2CO_3	CH_2Cl_2	78	97
18	QN-**3f**[d]	Cs_2CO_3	CH_2Cl_2	56	96[f]
19[g]	QD-**3f**[d]	Cs_2CO_3	CH_2Cl_2	80	97

[a] Reactions were carried out with FBSM (1.0 equiv), **1a** (1.1 equiv), base (3.0 equiv), and catalyst (10 mol%) in solvent at −40°C for 1 d unless otherwise noted. Yields were calculated based on FBSM. [b] Yield of isolated product. [c] X = Cl. [d] X = Br. [e] 10 equiv of K_2CO_3 was used. [f] (*R*)-**2a** was obtained. [g] 5 mol% of QD-**3f** was used.

Table 2: Substrate scope for 1,4-addition reaction.[a]



Entry	**1**	Ar	R	**2**[b]	Yield[c] [%]	*ee* [%]
1	**1a**	Ph	Ph	(*S*)-**2a**	80	97
2	**1b**	Ph	4-ClC_6H_4	(*S*)-**2b**	76	97
3	**1c**	Ph	3-ClC_6H_4	(*S*)-**2c**	85	98
4	**1d**	Ph	4-BrC_6H_4	(*S*)-**2d**	86	97
5	**1e**	Ph	4-MeC_6H_4	(*S*)-**2e**	77	94
6	**1f**	4-ClC_6H_4	Ph	(*S*)-**2f**	52	91
7	**1g**	4-BrC_6H_4	Ph	(*S*)-**2g**	82	95
8	**1h**	4-$BocOC_6H_4$	4-BrC_6H_4	(*S*)-**2h**	32	95
9	**1i**	Ph	Me	(*R*)-**2i**	91	85
10	**1j**	Ph	Et	(*R*)-**2j**	69	90
11[d]	**1a**	Ph	Ph	(*R*)-**2a**	58	96
12[d]	**1b**	Ph	4-ClC_6H_4	(*R*)-**2b**	64	96
13[d]	**1c**	Ph	3-ClC_6H_4	(*R*)-**2c**	77	82
14[d]	**1d**	Ph	4-BrC_6H_4	(*R*)-**2d**	90	94
15[d]	**1f**	4-ClC_6H_4	Ph	(*R*)-**2f**	90	89
16[d]	**1g**	4-BrC_6H_4	Ph	(*R*)-**2g**	68	93
17[d]	**1j**	Ph	Et	(*S*)-**2j**	56	84

[a] Reactions were carried out using FBSM (1.0 equiv), **1** (1.1 equiv), Cs_2CO_3 (3.0 equiv), and QD-**3f** (X = Br; 5 mol%) in CH_2Cl_2 at −40°C for 1–2 d. Yields were calculated based on FBSM unless otherwise noted. [b] The absolute stereochemistry of (*S*)-**2a** was determined by X-ray crystallographic analysis and all other products were tentatively assigned by analogy. [c] Yield of isolated product. [d] QN-**3f** (X = Br; 5 mol%) was used as a catalyst.

With optimal conditions in hand, the scope of the FBSM-based Michael addition reaction was explored with a variety of substrates to establish the generality of the process. By using a catalytic amount of QD-**3f** (X = Br; 5 mol%), all substrates afforded products in good to excellent yield and high to excellent enantioselectivity (Table 2). A series of chalcone derivatives (**1a–h**) with a variety of substituents, such as bromo, chloro, methyl, and *O*-Boc groups, on their aromatic rings were nicely converted into products **2a–h** in good yields with *ee* values ranging from 91 to 98% (Table 2, entries 1–8). Enolizable enones **1i** and **1j** were also compatible with the same reaction conditions and afforded products **2i** and **2j** in good yield with *ee* values of 85% and 90%, respectively (Table 2, entries 9 and 10). The absolute stereochemistry of (*S*)-**2a** was determined by an X-ray crystallographic analysis (see the Supporting Information) and all the other products are tentatively assigned by analogy to that of **2a**. Compound QN-**3f** (X = Br) was also found to be a general catalyst, furnishing the antipode of **2** in high yield with excellent enantioselectivity (Table 2, entries 11–17).

To understand the high enantioselectivity observed for the conjugate addition catalyzed by the cinchona alkaloids QD-**3f** (X = Br) and QN-**3f** (X = Br), both of which have a bulky benzyl substituent on the quaternary nitrogen atom, we postulated a transition-state structure for the production of (*R*)-**2a** catalyzed by QN-**3f** (Figure 1). The three-dimensional molecular structure of QN-**3f** was generated by the PM3 method of the MOPAC program together with the X-ray crystallographic data reported for the QN-**3a**·Cl/malonic acid complex,[13] which indicated that QN-**3f** exists in an open conformation[14] (Figure 1a). The free hydroxy group in QN-**3f** captures substrate **1a**, presumably by intermolecular hydrogen-bond formation to the carbonyl oxygen atom in **1a** (Figure 1b). This hypothesis would be consistent with participation of the chloride in a hydrogen bond with the OH group of QN-**3f** as observed in the calculated structure in Figure 1a. The aromatic π–π interactions between **1a** and QN-**3f** additionally stabilize the transition-state structure in which the FBSM approaches from the *Re* face of **1a**; the *Si* face is effectively blocked by the bulky parts of the benzyl substituent in QN-**3f** (Figure 1b).

The conjugate addition adducts (**2**) can be readily converted into the respective monofluoromethylated derivatives (**6**) by a sequence of steps without racemization (Scheme 1): 1) $NaBH_4$-reduction of the carbonyl group of

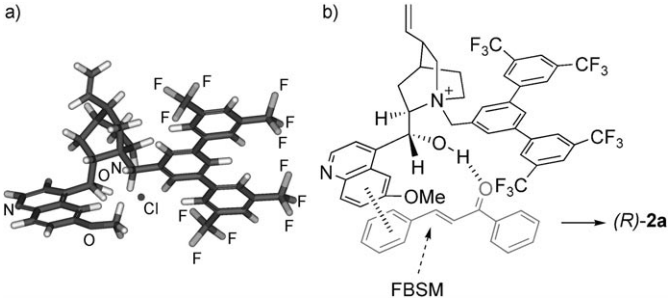
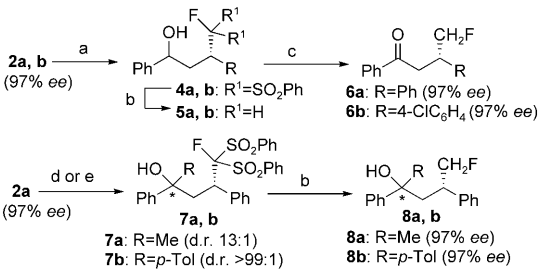


Figure 1. a) Three-dimensional structure of QN-**3f** (X = Cl; calculated). b) A proposed transition-state assembly for the enantioselective Michael addition of FBSM to **1a** catalyzed by QN-**3f** (X = Br) to give (*R*)-**2a**.



Scheme 1. Conversions of 1,4-addition products into monofluoromethylated compounds. a) $NaBH_4$ (1.2 equiv), THF/MeOH (8:1), RT, 1 h, 98% for **4a**, 98% for **4b**; b) Mg (10 equiv), THF/MeOH (1:4), 0 °C → RT, 1 h, 50% for **5a**, 72% for **5b**, 50% for **8a**, 54% for **8b**; c) PCC (2.0 mol%), H_5IO_6 (1.05 equiv), MeCN, 97% for **6a**, 70% for **6b**; d) MeMgBr (5.0 equiv), THF, −60 → −40 °C, 83%, d.r. 13:1, for **7a**; e) *p*-TolMgBr (5.0 equiv), THF, −20 → 0 °C, 70%, d.r. > 99:1, for **7b**. PCC = pyridinium chlorochromate.

2a and **b** to alcohols **4a** and **b**, respectively, 2) reductive desulfonylation to **5a** and **b** using Mg/MeOH, and 3) PCC oxidation of **5a** and **b**. Notably, an additional stereocenter can be constructed with high diastereoselectivity by the addition of a methyl or tolyl Grignard reagent to **2a** (d.r. 13:1 for MeMgBr, d.r. > 99:1 for *p*-TolMgBr) and subsequent desulfonylation using Mg/MeOH to afford monofluorinated derivatives **8a**, **b** in good yields without any loss of the chiral information at the benzylic positions. The absolute stereochemistry at the newly generated quaternary carbon center of **8** was not determined.

In summary, we have used the ammonium salts of sterically demanding cinchona alkaloids QD-**3f** and QN-**3f** to promote the first asymmetric conjugate addition of FBSM to α,β-unsaturated ketones, providing versatile and enantiomerically enriched adducts. A wide substrate scope, a high level of enantioselectivity, and the flexibility to generate either enantiomer of the product have been achieved. The conjugate addition adducts are useful for the synthesis of chiral monofluoromethylated molecules. Additional investigations of the full scope of this conjugate addition reaction and applications to the synthesis of biologically interesting targets are underway in our laboratory.

Experimental Section

1a (0.385 mmol, 80.2 mg) was added to a stirred mixture of FBSM (0.350 mmol, 110.0 mg), QD-**3f** (0.0175 mmol, 16.1 mg), and Cs_2CO_3 (1.05 mmol, 342.1 mg) in dry CH_2Cl_2 (1.0 mL) at −40 °C. After completion of the reaction (1–2 days, monitored by TLC), the reaction mixture was diluted with CH_2Cl_2 and then washed with water and brine. The organic layer was dried over Na_2SO_4 and the solvent was then removed under reduced pressure. After purification by chromatography on silica gel eluting with acetone in hexane (2:8), **2a** was obtained as a colorless solid (145.7 mg, 80%). The *ee* value was determined to be 97% by using HPLC analysis (DAICEL CHIRAL CEL AD-H column; *i*PrOH/hexane 3:7).

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[1] a) P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, Weinheim, **2004**; b) *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications* (Eds.: R. Filler, Y. Kobayashim, L. M. Yagupolskii), Elsevier, Amsterdam, **1993**.
[2] D. B. Harper, D. O'Hagan, *Nat. Prod. Rep.* **1994**, *11*, 123–133.
[3] a) *Fusso Yakugaku* (Eds.: Y. Kobayashi, I. Kumadaki, T. Taguchi), Hirokawa, Tokyo, **1992**; b) J. Kollonitsch, *Biomedicinal Aspects of Fluorine Chemistry*, Elsevier Biomedical Press and Kodansha Ltd, New York, **1982**, 93–122; c) *Organofluorine Chemistry, Principles and Commercial Applications* (Eds.: R. E. Banks, B. E. Smart, J. C. Tatlow), Plenum, New York, **1994**, chap. 3; d) B. E. Smart, *J. Fluorine Chem.* **2001**, *109*, 3–11; e) K. L. Kirk, *J. Fluorine Chem.* **2006**, *127*, 1013–1029; f) D. O'Hagan, H. S. Rzepa, *Chem. Commun.* **1997**, 645–652.
[4] a) J. Kollonitsch, A. A. Patchett, S. Marburg, A. L. Maycock, L. M. Perkins, G. A. Doldouras, D. E. Duggan, S. D. Aster, *Nature* **1978**, *274*, 906–908; b) G. L. Grunewald, T. M. Caldwell, Q. Li, M. Slavica, K. R. Criscione, R. T. Borchardt, W. Wang, *J. Med. Chem.* **1999**, *42*, 3588–3601; c) R. B. Silverman, S. M. Nanavati, *J. Med. Chem.* **1990**, *33*, 931–936; d) P. Bey, F. Gerhart, V. V. Dorsselaer, C. Danzin, *J. Med. Chem.* **1983**, *26*, 1551–1556; e) G. L. Grunewald, M. R. Seim, R. C. Regier, J. L. Martin, L. Gee, N. Drinkwater, K. R. Criscione, *J. Med. Chem.* **2006**, *49*, 5424–5433; f) G. W. Gribble, *J. Chem. Educ.* **1973**, *50*, 460–462; g) R. Peters, R. W. Wakelin, *Proc. R. Soc. London Ser. B* **1953**, *140*, 497–507; h) E. Kun, R. J. Dummel, *Methods Enzymol.* **1969**, *13*, 623–672.
[5] a) J.-A. Ma, D. Cahard, *Chem. Rev.* **2004**, *104*, 6119–6146; b) H. Ibrahim, A. Togni, *Chem. Commun.* **2004**, 1147–1155; c) M. Oestreich, *Angew. Chem.* **2005**, *117*, 2376–2379; *Angew. Chem. Int. Ed.* **2005**, *44*, 2324–2327; d) P. M. Pihko, *Angew. Chem.* **2006**, *118*, 558–561; *Angew. Chem. Int. Ed.* **2006**, *45*, 544–547; e) C. Bobbio, V. Gouverneur, *Org. Biomol. Chem.* **2006**, *4*, 2065–2075; f) N. Shibata, *J. Synth. Org. Chem. Jpn.* **2006**, *64*, 14–24; g) N. Shibata, T. Ishimaru, S. Nakamura, T. Toru, *J. Fluorine Chem.* **2007**, *128*, 469–483; h) Y. Hamashima, M. Sodeoka, *J. Synth. Org. Chem. Jpn.* **2007**, *64*, 1099–1107; i) V. A. Brunet, D. O'Hagan, *Angew. Chem.* **2008**, *120*, 1198–1201; *Angew. Chem. Int. Ed.* **2008**, *47*, 1179–1182; j) S. Bruns, G. Haufe, *J. Fluorine Chem.* **2000**, *104*, 247–254; k) G. Haufe, S. Bruns, *Adv. Synth. Catal.* **2002**, *344*, 165–171.
[6] a) N. Shibata, T. Ishimaru, T. Nagai, J. Kohno, T. Toru, *Synlett* **2004**, 1703–1706; b) N. Shibata, J. Kohno, K. Takai, T. Ishimaru, S. Nakamura, T. Toru, S. Kanemasa, *Angew. Chem.* **2005**, *117*, 4276–4279; *Angew. Chem. Int. Ed.* **2005**, *44*, 4204–4207; c) N.

Shibata, H. Yasui, S. Nakamura, T. Toru, *Synlett* **2007**, 1153 – 1157; d) D. S. Reddy, N. Shibata, J. Nagai, S. Nakamura, T. Toru, *Angew. Chem.* **2008**, *120*, 170 – 174; *Angew. Chem. Int. Ed.* **2008**, *47*, 164 – 168; e) T. Ishimaru, N. Shibata, T. Horikawa, N. Yasuda, S. Nakamura, T. Toru, M. Shiro, *Angew. Chem.* **2008**, *120*, 4225 – 4229; *Angew. Chem. Int. Ed.* **2008**, *47*, 4157 – 4161.

[7] a) J.-A. Ma, D. Cahard, *J. Fluorine Chem.* **2007**, *128*, 975 – 996; b) T. Billard, B. R. Langlois, *Eur. J. Org. Chem.* **2007**, 891 – 897; c) N. Shibata, S. Mizuta. T. Toru, *J. Synth. Org. Chem. Jpn.* **2008**, *66*, 215 – 218.

[8] a) T. Fukuzumi, N. Shibata, M. Sugiura, H. Yasui, S. Nakamura, T. Toru, *Angew. Chem.* **2006**, *118*, 5095 – 5099; *Angew. Chem. Int. Ed.* **2006**, *45*, 4973 – 4977; b) S. Mizuta, N. Shibata, Y. Goto, T. Furukawa, S. Nakamura, T. Toru, *J. Am. Chem. Soc.* **2007**, *129*, 6394 – 6395.

[9] a) C. Ni, Y. Li, J. Hu, *J. Org. Chem.* **2006**, *71*, 6829 – 6833; b) G. K. S. Prakash, S. Chacko, S. Alconcel, T. Stewart, T. Mathew, G. A. Olah, *Angew. Chem.* **2007**, *119*, 5021 – 5024; *Angew. Chem. Int. Ed.* **2007**, *46*, 4933 – 4936.

[10] a) M. Shibasaki, N. Yoshikawa, *Chem. Rev.* **2002**, *102*, 2187 – 2209; b) K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013 – 3028; c) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656 – 5682.

[11] Just before the submission of our manuscript, Prakash, Olah and co-workers reported the (racemic) conjugate addition of FBSM to α,β-unsaturated ketones by using either phosphines or potassium carbonate: G. K. S. Prakash, X. Zhao, S. Chacko, F. Wang, H. Vaghoo, G. A. Olah, *Beilstein J. Org. Chem.* **2008**, DOI: 10.3762/bjoc.4.17.

[12] Mukaiyama and co-workers reported the phenoxide salts of CN-**3f** (X = OPh) and CD-**3f** for asymmetric reactions: a) T. Tozawa, H. Nagao, Y. Yamane, T. Mukaiyama, *Chem. Asian J.* **2007**, *2*, 123 – 134; b) H. Nagao, Y. Kawano, T. Mukaiyama, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 2406 – 2412; c) H. Nagao, Y. Yamane, T. Mukaiyama, *Chem. Lett.* **2007**, *36*, 666 – 667; d) H. Nagao, Y. Yamane, T. Mukaiyama, *Heterocycles* **2007**, *72*, 553 – 565; e) T. Mukaiyama, H. Nagao, Y. Yamane, *Chem. Lett.* **2006**, *35*, 916 – 917.

[13] W. Zhang, S. Wu, Z. Zhang, H. Yennawar, X. Zhang, *Org. Biomol. Chem.* **2006**, *4*, 4474 – 4477.

[14] a) G. D. H. Dijkstra, R. M. Kellogg, H. Wynberg, *Recl. Trav. Chim. Pays-Bas* **1989**, *108*, 195 – 204; b) G. D. H. Dijkstra, R. M. Kellogg, H. Wynberg, J. S. Svendsen, I. Marko, K. B. Sharpless, *J. Am. Chem. Soc.* **1989**, *111*, 8069 – 8076; c) T. Burgi, A. Baiker, *J. Am. Chem. Soc.* **1998**, *120*, 12920 – 12926; d) N. Shibata, E. Suzuki, T. Asahi, M. Shiro, *J. Am. Chem. Soc.* **2001**, *123*, 7001 – 7009.

[15] During the review of this manuscript, Hu and co-workers reported the (racemic) conjugate addition of FBSM to α,β-enones by using NaOH. C. Ni, L. Zhang, J. Hu, *J. Org. Chem.* **2008**, *73*, 5699 – 5713.

