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Organocatalytic asymmetric allylic alkylation of sulfonylimidates with Morita-Baylis-Hillman carbonates

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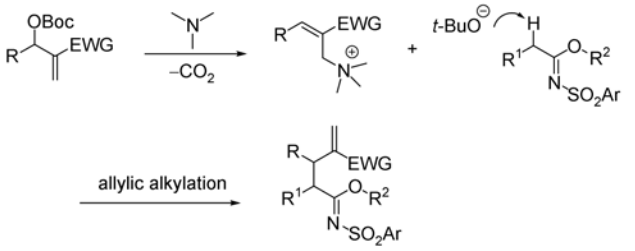
The asymmetric allylic alkylation reaction of sulfonylimidates with various Morita-Baylis-Hillman (MBH) carbonates was accomplished by the catalysis of commercially available cinchona alkaloids catalyst $(DHQD)_2AQN$. The corresponding allylic alkylation products were obtained in good yields with high stereoselectivities (up to 99% ee, 89∶11 dr).

organocatalysis, asymmetric allylic alkylation, sulfonylimidates, Morita-Baylis-Hillman carbonates, cinchona alkaloids

1 Introduction

Imidates, also known as imidoates, imidic acid esters, or imido esters, are known to be important pharmacophores and useful synthetic building blocks [1–3]. Recently, the transformations of imidates have received increasing attention and much efforts have been devoted to this field [4–10]. Kobayashi group reported the first example of sulfonylimidates acting as nucleophiles in catalytic addition reaction with imines [4]. Later, a Pd/Brønsted base-catalyzed approach to the decarboxylative allylation of sulfonylimidates has been developed [5, 6]. In addition, the first example of a catalytic asymmetric Mannich-type reaction of a sulfonylimidate has been reported, which was catalyzed by alkaline earth metals, but only moderate enantioselectivity was observed [7]. A notable example was reported by Barbas *et al*. who developed a stereoselective organocatalytic Michael addition of *N*-tosylimidates to α,β-unsaturated aldehydes catalyzed by trialkylsilyl-protected α,α-diarylprolinol [8]. However, there were limitations for the chemical yields, diastereomeric ratios and generality of the substrates. The optimization of the asymmetric variant as well as the application of sulfonylimidates is still far from satisfaction. Therefore, it is desirable to find out a mild and efficient process for the direct asymmetric modification of sulfonylimidates.

Recently, the allylic alkylation of Morita-Baylis-Hillman (MBH) adducts catalyzed by a metal-free organic Lewis base has emerged as an attractive strategy to prepare multifunctional compounds [11–22]. Our group have also reported that modified cinchona alkaloids can act as excellent organocatalysts for asymmetric allylic alkylation (AAA) reactions with MBH carbonates [23–28]. On the other hand, the deprotonation of α-position from a carbonyl compound and the subsequent nucleophilic addition of the formed enolate is a fundamental sequence of transformations in



Scheme 1 Proposed allylic alkylation of sulfonylimidates with MBH carbonates catalyzed by tertiary amine.

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synthetic organic chemistry. In general, a stoichiometric amount of base is necessary in the deprotonation step. So we anticipated that, as outlined in Scheme 1, the deprotonation of the α-H of the sulfonylimidates by the *tert*-butoxy anion generated in suit would occur, and the subsequent asymmetric allylic alkylation would follow to deliver valuable chiral sulfonylimidate derivatives.

2 Experimental

2.1 General methods

NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (200–300 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H NMR spectra were recorded at 400 MHz (Varian), and ^{13}C NMR spectra were recorded at 50 MHz or 100 MHz (Varian). Chemical shifts were reported in ppm downfield from $CDCl_3$ (δ 7.27 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ 77.0 ppm) for ^{13}C NMR spectroscopy. Coupling constants were given in Hz. Optical rotations were measured at 589 nm, 20 °C. Enantiomeric excess was determined by HPLC analysis on Chiralpak AS, IC, AD and Chiralcel OD columns. Toluene was distilled from CaH_2. All other chemicals were used without purification as commercially available. Cinchona alkaloids catalysts $(DHQD)_2PHAL$, $(DHQD)_2PYR$, $(DHQD)_2AQN$, $(DHQ)_2AQN$ were purchased from Aldrich Chemical Company.

2.2 General procedure for asymmetric allylic alkylation of sulfonylimidates 1 and Morita-Baylis-Hillman carbonates 2

A mixture of sulfonylimidate **1** (0.1 mmol), Morita-Baylis-Hillman carbonate **2** (0.2 mmol) and $(DHQD)_2AQN$ (10 mol%) in dry toluene (1.0 mL) were stirred at 50 °C for a specified reaction time. Then the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate) to give the product **3**.

Compound 3c. 98% yield; 87:13 dr; $[\alpha]_D^{20}$ = −105.9 (*c* = 1.0 in $CHCl_3$); 96% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, *t*(major) = 12.06 min, *t*(minor) = 17.96 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.44 (m, 4H), 7.33–7.29 (m, 2H), 7.26–7.21 (m, 4H), 7.15–7.06 (m, 6H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.57 (s, 1H), 6.49 (s, 1H), 5.52 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 12.0 Hz, 1H), 3.71 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 166.8, 151.6, 143.1, 141.8, 138.5, 135.4, 129.3, 129.3, 129.1, 128.6, 128.5, 128.1, 127.9, 127.3, 126.8, 126.3, 126.0, 125.3, 120.9, 53.6, 52.2, 49.7, 21.4 ppm; ESI-HRMS: calcd for $C_{27}H_{27}NO_5S$+Na 500.1508, found 500.1517.

Compound 3d. 98% yield; 87:13 dr; $[\alpha]_D^{20}$ = −130.3 (*c* = 0.40 in $CHCl_3$); 95% ee, determined by HPLC analysis [Daicel chiralpak IC, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, *t*(major) = 19.80 min, *t*(minor) = 22.14 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.43 (m, 4H), 7.32–7.30 (m, 2H), 7.28–7.08 (m, 4H), 7.12–7.02 (m, 6H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.58 (s, 1H), 6.48 (s, 1H), 5.47 (d, *J* = 12.0 Hz, 1H), 4.90 (d, *J* = 12.0 Hz, 1H), 3.71 (s, 3H), 2.32 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 166.6, 151.5, 143.2, 141.5, 138.3, 137.2, 135.1, 132.7, 129.9, 129.4, 129.2, 129.1, 128.6, 128.3, 128.1, 126.4, 126.3, 125.6, 121.0, 53.4, 52.2, 49.1, 21.4 ppm; ESI-HRMS: calcd for $C_{32}H_{28}ClNO_5S$+Na 596.1274, found 596.1293.

Compound 3e. 82% yield; 87:13 dr; $[\alpha]_D^{20}$ = −107.3 (*c* = 0.95 in $CHCl_3$); 97% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, *t*(major) = 10.05 min, *t*(minor) = 14.15 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.43 (m, 4H), 7.32–7.28 (m, 2H), 7.23–7.15 (m, 4H), 7.13–7.05 (m, 2H), 7.00–6.87 (m, 6H), 6.56 (s, 1H), 6.47 (s, 1H), 5.49 (d, *J* = 12.0 Hz, 1H), 4.89 (d, *J* = 12.0 Hz, 1H), 3.70 (s, 3H), 3.33 (s, 3H), 2.19 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 166.8, 151.6, 143.1, 141.8, 138.4, 137.6, 135.5, 129.3, 129.3, 129.1, 128.6, 128.4, 127.9, 127.8, 127.6, 127.2, 126.3, 125.8, 125.4, 123.6, 121.1, 53.7, 52.2, 49.5, 21.4, 21.3 ppm; ESI-HRMS: calcd for $C_{33}H_{31}NO_5S$+Na 576.1821, found 576.1812.

Compound 3f. 86% yield; 86:14 dr; $[\alpha]_D^{20}$ = −120.0 (*c* = 0.95 in $CHCl_3$); 98% ee, determined by HPLC analysis [Daicel Chiralcel OD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, *t*(major) = 11.20 min, *t*(minor) = 15.59 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.43 (m, 4H), 7.32–7.29 (m, 2H), 7.24–7.15 (m, 4H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 6.53 (s, 1H), 6.44 (s, 1H), 5.46 (d, *J* = 11.2 Hz, 1H), 4.87 (d, *J* = 12.0 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 2.32 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.6, 166.9, 158.4, 151.7, 143.1, 142.2, 138.5, 135.7, 130.6, 130.1, 129.6, 129.4, 129.1, 128.9, 128.5, 127.8, 126.3, 124.9, 121.1, 113.6, 55.1, 53.8, 52.1, 49.0, 21.4 ppm; ESI-HRMS: calcd for $C_{33}H_{31}NO_6S$+Na 592.1770, found 592.1757.

Compound 3g. 94% yield; 89:11 dr; $[\alpha]_D^{20}$ = −69.5 (*c* = 0.44 in $CHCl_3$); 93% ee, determined by HPLC analysis [Daicel chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, *t*(major) = 16.57 min, *t*(minor) = 18.39 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.42 (m, 5H), 7.35–7.30 (m, 3H), 7.28–7.24 (m, 2H), 7.22–7.13 (m, 3H), 6.96–6.95 (m, 2H), 6.94–6.61 (m, 3H), 6.49 (s, 1H), 6.39 (s, 1H), 5.55 (br s, 2H), 3.72 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.0, 166.6, 151.6, 143.1, 138.4, 138.0, 134.2, 133.0, 130.1, 129.7, 129.4, 129.1, 128.8, 128.4, 128.2, 128.1, 127.4, 126.5, 126.3, 126.0, 121.2, 53.5, 52.1, 49.6, 21.4 ppm; ESI-HRMS: calcd for $C_{32}H_{28}BrNO_5S$+H 618.0950,

found 618.0944.

Compound 3h. 99% yield; 67:33 dr; $[\alpha]_D^{20}$ = −25.1 (*c* = 0.52 in $CHCl_3$); 90% ee, determined by HPLC analysis [Daicel chiralpak IC, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, *t*(major) = 29.11 min, *t*(minor) = 26.98 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.53 (m, 2H), 7.50–7.48 (m, 2H), 7.37–7.26 (m, 7H), 7.25–7.16 (m, 2H), 7.15–7.11 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.59 (s, 1H), 6.47 (s, 1H), 5.89 (d, *J* = 2.8 Hz, 1H), 5.07 (d, *J* = 12.0 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 166.7, 151.3, 143.1, 141.9, 138.8, 129.6, 129.3, 129.1, 128.9, 128.8, 128.6, 128.1, 127.7, 126.4, 126.3, 121.0, 110.1, 108.1, 52.3, 51.9, 42.9, 21.4 ppm; ESI-HRMS: calcd for $C_{30}H_{27}NO_6S$+H 530.1637, found 530.1649.

Compound 3i. 93% yield; 68:32 dr; $[\alpha]_D^{20}$ = −69.1 (*c* = 0.75 in $CHCl_3$); 92% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, *t*(major) = 13.55 min, *t*(minor) = 23.85 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.53 (m, 2H), 7.49 (d, *J* = 4.8 Hz, 2H), 7.34–7.15 (m, 6H), 7.14–7.09 (m ,2H), 7.05–7.01 (m, 1H), 6.86–6.84 (m, 2H), 6.73–6.71 (m, 1H), 6.60 (s, 1H), 6.46 (s, 1H), 5.52 (d, *J* = 12.0 Hz, 1H), 5.23 (d, *J* = 12.0 Hz, 1H), 3.75 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.7, 166.6, 151.5, 143.2, 142.4, 141.8, 138.4, 135.5, 129.4, 129.4, 129.1, 129.0, 128.8, 128.7, 128.2, 126.5, 126.4, 126.3, 124.6, 121.0, 54.5, 52.3, 44.7, 21.4 ppm; ESI-HRMS: calcd for $C_{30}H_{27}NO_5S_2$+Na 568.1228, found 568.1219.

Compound 3j. 99% yield; 84:16 dr; $[\alpha]_D^{20}$ = −65.0 (*c* = 1.00 in $CHCl_3$); 99% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, *t*(major) = 8.28 min, *t*(minor) = 13.32 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.46 (m, 4H), 7.31–7.26 (m, 2H), 7.21–7.17 (m, 4H), 7.13–7.03 (m, 7H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.72 (s, 1H), 6.42 (s, 1H), 5.54 (d, *J* = 12.0 Hz, 1H), 5.13 (d, *J* = 12.0 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 198.1, 172.3, 151.5, 149.9, 143.1, 138.9, 135.5, 129.3, 129.3, 129.1, 128.6, 128.5, 128.1, 127.8, 127.7, 126.7, 126.3, 126.2, 125.6, 121.0, 53.5, 47.4, 25.9, 21.4 ppm; ESI-HRMS: calcd for $C_{32}H_{29}NO_4S$+H 524.1896, found 524.1897.

Compound 3k. 88% yield; 87:13 dr; $[\alpha]_D^{20}$ = +45.3 (*c* = 0.86 in $CHCl_3$); 73% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, *t*(major) = 13.67 min, *t*(minor) = 8.45 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.43–7.32 (m, 5H), 7.26–7.10 (m, 11H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.51 (s, 1H), 6.17 (s, 1H), 5.52 (br s, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 2.35 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 151.3, 143.4, 138.0, 136.0, 134.3, 131.4, 130.8, 129.5, 129.2, 128.7, 128.4, 128.2, 127.9, 127.6, 126.9, 126.5, 125.0, 121.1, 118.3, 53.2, 52.3, 21.5 ppm; ESI-HRMS: calcd for $C_{31}H_{26}N_2O_3S$+H 507.1742, found 507.1742.

Compound 3l, diastereomer 1. 34% yield; $[\alpha]_D^{20}$ = −11.1 (*c* = 0.35 in $CHCl_3$); 81% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, *t*(major) = 10.52 min, *t*(minor) = 9.27 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 7.49–7.48 (m, 2H), 7.39–7.32 (m, 6H), 7.23–7.21 (m, 2H), 5.98 (s, 1H), 5.83 (s, 1H), 5.08 (s, 2H), 5.01 (d, *J* = 12.0 Hz, 1H), 3.00-2.94 (m, 1H), 1.37-1.29 (m, 2H), 0.78 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.8, 134.7, 133.6, 132.9, 129.1, 128.9, 128.8, 128.6, 128.6, 128.1, 124.1, 124.0, 117.6, 71.5, 53.1, 48.7, 23.9, 10.8 ppm; ESI-HRMS: calcd for $C_{27}H_{25}N_3O_5S$+Na 526.1413, found 526.1424.

Compound 3l, diastereomer 2. 34% yield; $[\alpha]_D^{20}$ = +17.6 (*c* = 0.25 in $CHCl_3$); 81% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, *t*(major) = 15.29 min, *t*(minor) = 12.36 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, *J* = 8.8 Hz, 2H), 8.02 (d, *J* = 8.8 Hz, 2H), 7.46–7.44 (m, 2H), 7.40–7.30 (m, 6H), 7.26–7.20 (m, 2H), 5.70 (s, 1H), 5.47 (s, 1H), 5.20 (d, *J* = 12.0 Hz, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 4.97(d, *J* = 12.0 Hz, 1H), 2.94 (dt, *J* = 7.2, 2.8 Hz, 1H), 1.72–1.64 (m, 1H), 1.58-1.46 (m, 1H), 0.89 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 134.5, 133.8, 133.7, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.5, 128.4, 128.1, 124.1, 122.8, 116.5, 71.3, 53.7, 50.6, 24.9, 11.7 ppm; ESI-HRMS: calcd for $C_{27}H_{25}N_3O_5S$+Na 526.1413, found 526.1385.

Compound 3m. 97% yield; 85:15 dr; $[\alpha]_D^{20}$ = −164.3 (*c* = 0.46 in $CHCl_3$); 91% ee, determined by HPLC analysis [Daicel chiralpak AS, *n*-hexane/*i*-PrOH=80/20, 1.0 mL/min, λ = 254 nm, *t*(major) = 9.09 min, *t*(minor) =14.91 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.0 Hz, 2H), 8.30 (d, *J* = 8.0 Hz, 2H), 7.36–7.28 (m, 3H), 7.26–7.21 (m, 4H), 7.14–7.13 (m, 3H), 7.10–7.05 (m, 3H), 7.02–7.00 (m, 2H), 6.41 (s, 1H), 6.32 (s, 1H), 5.36 (d, *J* = 12.0 Hz, 1H), 5.19 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 3.63 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 166.4, 149.8, 146.9, 141.7, 138.1, 135.0, 133.6, 129.1, 128.8, 128.5, 128.5, 128.4, 128.1, 127.9, 127.8, 127.6, 126.8, 124.8, 123.9, 71.3, 54.4, 52.0, 49.4 ppm; ESI-HRMS: calcd for $C_{32}H_{28}N_2O_7S$+Na 607.1515, found 607.1512.

Compound 3n. 72% yield; $[\alpha]_D^{20}$ = −131.9 (*c* = 0.70 in $CHCl_3$); 88% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, *t*(major) = 9.79 min, *t*(minor) =13.75 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.30–7.19 (m, 10H), 7.05–7.03 (m, 2H), 6.32 (s, 1H), 5.74 (s, 1H), 4.96 (s, 2H), 4.58 (t, *J* = 8.0 Hz, 1H), 3.64 (s, 3H), 3.62–3.58 (m, 1H), 3.51–3.45 (m, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.7, 141.8, 140.5, 131.0, 129.4, 128.6, 128.4, 127.9, 127.6, 126.9, 125.5, 118.9,

108.9, 70.3, 51.9, 42.5, 38.2, 21.5 ppm; ESI-HRMS: calcd for $C_{27}H_{27}NO_5S$+Na 500.1508, found 500.1517.

Compound 3o, diastereomer 1. 33% yield; $[\alpha]_D^{20}$ = –16.8 (c = 0.25 in $CHCl_3$); 93% ee, determined by HPLC analysis [Daicel Chiralcel OD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, t(major) = 6.30 min, t(minor) = 5.35 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.8 Hz, 2H), 7.82 (d, J = 8.8 Hz, 2H), 7.39–7.13 (m, 5H), 6.45 (s, 1H), 5.99 (s, 1H), 4.54 (dt, J = 6.8, 3.2 Hz, 1H), 4.23 (d, J = 12.0 Hz, 1H), 4.02–3.94 (m, 1H), 3.80–3.75 (m, 1H), 3.71 (s, 3H), 1.85–1.73 (m, 1H), 1.71–1.64 (m, 1H), 1.47–1.37 (m, 2H), 1.33–1.30 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 177.4, 166.1, 147.8, 142.4, 139.8, 128.7, 128.5, 127.9, 127.2, 126.6, 125.1, 124.1, 65.0, 52.0, 48.1, 47.6, 31.8, 28.4, 22.6, 13.7, 13.4 ppm; ESI-HRMS: calcd for $C_{25}H_{30}N_2O_7S$+Na 525.1671, found 525.1732.

Compound 3o, diastereomer 2. 33% yield; $[\alpha]_D^{20}$ = –65.7 (c = 0.30 in $CHCl_3$); 93% ee, determined by HPLC analysis [Daicel Chiralcel OD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, t(major) = 5.88 min, t(minor) = 6.71 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 8.8 Hz, 2H), 8.14 (d, J = 8.8 Hz, 2H), 7.39–7.24 (m, 5H), 6.31 (s, 1H), 6.26 (s, 1H), 4.34 (d, J = 12.0 Hz, 1H), 4.30–4.24 (m, 1H), 4.11 (q, J = 6.8 Hz, 2H), 3.68 (s, 3H), 1.51–1.42 (m, 1H), 1.15–1.10 (m, 1H), 1.25–1.19 (m, 7H), 0.76 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 177.4, 166.8, 147.7, 142.3, 139.7, 128.7, 128.5, 127.9, 127.2, 126.5, 125.1, 124.1, 65.0, 52.0, 48.0, 47.6, 31.7, 28.4, 22.6, 13.7, 13.4 ppm; ESI-HRMS: calcd for $C_{25}H_{30}N_2O_7S$+Na 525.1671, found 525.1662.

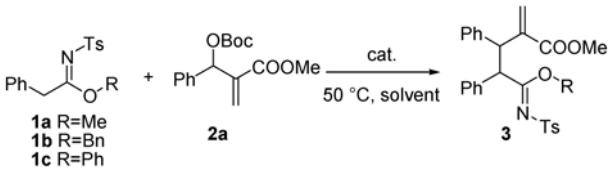
Compound 3p. 58% yield; 85:15 dr; $[\alpha]_D^{20}$ = –64.5 (c = 0.55 in $CHCl_3$); 96% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH=80/20, 1.0 mL/min, λ = 254 nm, t(major) = 6.99 min, t(minor) = 8.19 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 7.2 Hz, 2H), 8.15 (d, J = 7.2 Hz, 2H), 7.37–7.28 (m, 5H), 6.49 (s, 1H), 6.20 (s, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.30–4.24 (m, 1H), 4.12–4.04 (m, 2H), 2.24 (s, 3H), 1.62–1.46 (m, 2H), 1.24–1.09 (m, 7H), 0.76 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 197.9, 177.6, 150.3, 147.8, 140.1, 128.6, 128.4, 127.8, 127.4, 127.0, 125.7, 124.1, 64.9, 48.0, 45.3, 31.8, 28.5, 25.7, 22.6, 13.7, 13.5 ppm; ESI-HRMS: calcd for $C_{25}H_{30}N_2O_6S$+Na 509.1722, found 509.1723

3 Results and discussion

In the initial study, a range of commercially available modified cinchona alkaloids were screened in the AAA reaction of sulfonylimidate **1a** and MBH carbonate **2a** at 50 °C in DCE. To our gratification, the desired allylic product **3a** was isolated with good enantioselectivity and yield although with a moderate dr ratio by the catalysis of $(DHQD)_2AQN$ (Table 1, entry 1). Slightly lower enantioselectivities were obtained for the catalysis of $(DHQD)_2PHAL$ and $(DHQD)_2PYR$ (entries 2 and 3), but the diastereoselectivities were better. A poor ee value was obtained in the presence of $(DHQ)_2AQN$, while the product possesses the opposite configuration (entry 4). Subsequently, we further investigated the effects of solvents by the catalysis of $(DHQD)_2AQN$. Pleasingly, a higher ee value could be obtained in toluene and $PhCF_3$ (entries 5 and 6), and the reaction was slightly accelerated simultaneously. Longer reaction time was required at lower temperature, although the ee value was slightly improved (entry 7). Fortunately, better enantio- and diastereoselectivity were afforded when benzyl or phenyl esters were used (entries 8 and 9).

Having established the optimal reaction conditions, we next investigated the scope of this reaction (Table 2). Excellent ee values and good dr ratios were obtained for MBH carbonates bearing electron-withdrawing or -donating aryl groups (entries 2–5). In addition, heteroaryl-substituted MBH carbonates could be successfully applied, and excellent enantioselectivities were attained albeit with lower dr ratios (entries 6 and 7). Good results were also obtained with the MBH adduct from methyl vinyl ketone (entry 8). Besides, modest ee value and dr ratio were obtained for the MBH adduct from acrylonitrile (entry 9). It was noteworthy that the alkyl MBH adduct from acrylonitrile could be utilized in the AAA reaction though moderate ee value and poor diastereoselectivity were observed, while the two diastereomers could be separated (entry 10). *p*-Nitrophenylsulfonylimidate **1d** exhibited good reactivity with MBH carbonate **2a** and an excellent ee value with a good dr ratio were obtained (entry 11). Some substitutions at the α-posi-

Table 1 Screening studies of organocatalytic AAA reaction of sulfonylimidate **1** and MBH carbonate **2a**[a)]



Entry	Cat.	Sol	**1**	t (h)	Y [b)] (%)	ee [c)] (%)	dr [d)]
1	$(DHQD)_2AQN$	DCE	**1a**	32	89	84	73:27
2	$(DHQD)_2PHAL$	DCE	**1a**	42	85	79	90:10
3	$(DHQD)_2PYR$	DCE	**1a**	32	90	73	85:15
4	$(DHQ)_2AQN$	DCE	**1a**	22	98	–30	81:19
5	$(DHQD)_2AQN$	Tol	**1a**	21	92	90	73:27
6	$(DHQD)_2AQN$	$PhCF_3$	**1a**	21	94	89	72:28
7 [e]	$(DHQD)_2AQN$	Tol	**1a**	55	97	91	73:27
8	$(DHQD)_2AQN$	Tol	**1b**	24	92	92	83:17
9	$(DHQD)_2AQN$	Tol	**1c**	36	98	96	87:13

a) Unless noted otherwise, reactions were performed with 0.05 mmol **1**, 0.1mmol **2a** and 10 mol% catalyst in 0.5 mL solvent at 50 °C. b) Combined isolated yield of diastereomers. c) Determined by chiral HPLC analysis. d) Determined by ^{1}H NMR. e) At 35 °C.

tion of sulfonylimidates were also tested. Allylation of simple sulfonylimidate **1e** was achieved in good yield with a high ee (entry 12). For sulfonylimidate **1f** bearing longer carbon chain, stronger electron-withdrawing *N*-sulfonyl group was needed, and moderate yields and excellent enantioselectivities were observed (entries 13 and 14).

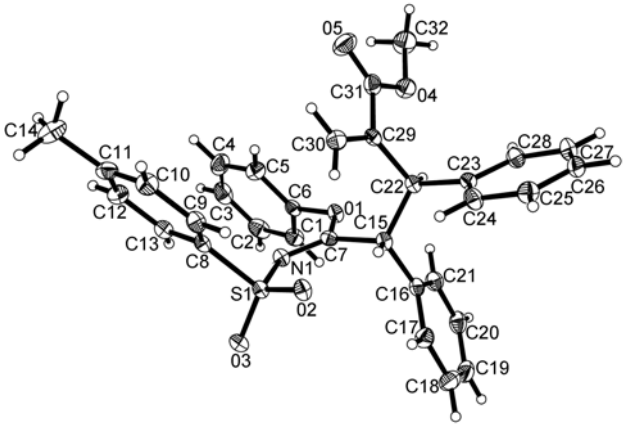
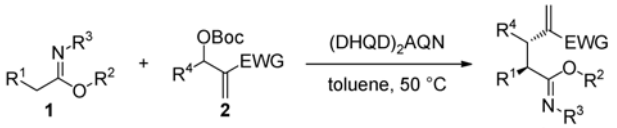


Figure 1 X-ray structure of enantiopure **3c**.

Table 2 Organocatalytic AAA reaction of sulfonylimidates **1** and MBH carbonates **2** [a)]



1c: R^1 = Ph, R^2 = Ph, R^3 = Ts
1d: R^1 = Ph, R^2 = Bn, R^3 = *p*-Ns
1e: R^1 = H, R^2 = Bn, R^3 = Ts
1f: R^1 = *n*Bu, R^2 = Et, R^3 = *p*-Ns

Entry	**1**	R^4	EWG	Yield [b)] (%)	Ee [c)] (%)	Dr [d)]
1	**1c**	Ph	COOMe	**3c**, 98	96[e]	87∶13
2	**1c**	*p*-ClC_6H_4	COOMe	**3d**, 98	95	87∶13
3	**1c**	*m*-MeC_6H_4	COOMe	**3e**, 82	97	87∶13
4	**1c**	*p*-$MeOC_6H_4$	COOMe	**3f**, 86	98	86∶14
5	**1c**	*o*-BrC_6H_4	COOMe	**3g**, 94	93	89∶11
6	**1c**	2-furyl	COOMe	**3h**, 99	90	67∶33
7	**1c**	2-thienyl	COOMe	**3i**, 93	92	68∶32
8	**1c**	Ph	COMe	**3j**, 99	99	84∶16
9	**1c**	Ph	CN	**3k**, 88	73	87∶13
10	**1d**	Me	CN	**3l**, 68	81/81	50∶50 [f)]
11	**1d**	Ph	COOMe	**3m**, 97	91	85∶15
12	**1e**	Ph	COOMe	**3n**, 72	88	–
13	**1f**	Ph	COOMe	**3o**, 66	93/93	50∶50 [f)]
14	**1f**	Ph	COMe	**3p**, 58 [g)]	96	85∶15

a) Unless noted otherwise, reactions were performed with 0.1 mmol **1**, 0.2 mmol **2** and 10 mol% $(DHQD)_2AQN$ in 1.0 mL toluene at 50 °C. b) Combined isolated yield of diastereomers. c) Determined by chiral HPLC analysis. d) Determined by ^1H NMR or HPLC analysis. e) The absolute configuration of major **3c** was determined by X-ray analysis, see Figure 1. The other major diastereomers were assigned accordingly. f) Calculated from the isolated yields of isomers. g) Isolated yield of the major diastereomer.

4 Conclusions

In conclusion, we have developed an organocatalytic asymmetric allylic alkylation of sulfonylimidates with Morita-Baylis-Hillman carbonates by the catalysis of commercially available modified cinchona alkaloids. Good stereoselectivities were generally achieved for a broad spectrum of substrates (dr up to 89:11, up to 99% ee). Currently further studies are underway to expand the synthetic utility of this reaction.

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