Tributyltin hydride-mediated radical cyclisation reactions: efficient construction of multiply substituted cyclopentanes†

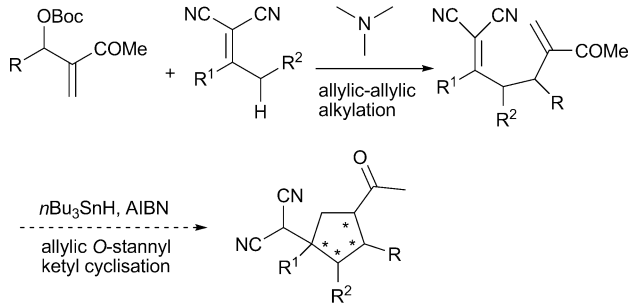
Jie Lei,[a,b] Hai-Lei Cui,[b] Rui Li,*[a] Li Wu,[b] Zheng-Yu Ding[a] and Ying-Chun Chen*[a,b]

Received 4th February 2010, Accepted 7th April 2010
First published as an Advance Article on the web 30th April 2010
DOI: 10.1039/c002378g

The nBu$_3$SnH-mediated cyclisation reactions of allylic-allylic alkylation products of α,α-dicyanoalkenes and Morita–Baylis–Hillman (MBH) carbonates of methyl vinyl ketone (MVK) have been investigated. Cyclopentane derivatives bearing multiple substituents were efficiently prepared with moderate to excellent diastereoselectivity.

Introduction

β-Hydroxyl-α-methylene compounds are multifunctional materials that receive continuing interest in organic synthesis. They are usually obtained *via* the so-called Morita–Baylis–Hillman (MBH) reaction, and considerable efforts have been devoted to this field over the past decades.[1] On the other hand, notable progress has been also made in view of the synthetic applications of MBH adducts.[2] Among them, the metal-free tertiary amine or phosphine-catalysed allylic alkylation of MBH carbonates or acetates has triggered special attention.[3,4] In particular, recently, we have developed a highly asymmetric allylic-allylic alkylation reaction of α,α-dicyanoalkenes and MBH carbonates, a following intramolecular Michael addition could afford *cyclohexenes* with multiple substitutions in a formal [3+3] annulation manner.[4a] In order to further expand their synthetic utilities, later we recognised the elegant work of Enholm, who reported tributyltin hydride-induced intramolecular cyclisation reactions of unsaturated ketones with electronically deficient olefins.[5] We envisaged that the similar tributyltin hydride-mediated cyclisation reactions should be developed with the allylic-allylic alkylation products from α,α-dicyanoalkenes and MBH carbonates of methyl vinyl ketone (MVK), as shown in Scheme 1, thus *cyclopentane* derivatives[6] bearing complex substitutions could be afforded in a straightforward way.[7]



Scheme 1 Radical cyclisation reaction to complex cyclopentane.

Results and discussion

Based on the above considerations, the initial study was conducted with racemic allylic-allylic adduct **1a** which was easily obtained by the catalysis of DABCO,[4a] under free radical cyclisation conditions reported by Enholm and co-workers.[5] To our gratification, the desired intramolecular cyclisation occurred smoothly in excellent diastereoselectivity, and a domino attack to one cyano group by the *O*-stannyl enolate intermediate happened to provide bridged cyclic enamine derivative **2a**, whose structure has been confirmed by X-ray crystallography analysis (Fig. 1)‡ (Table 1, entry 1, 66% yield, dr > 95 : 5).[8]

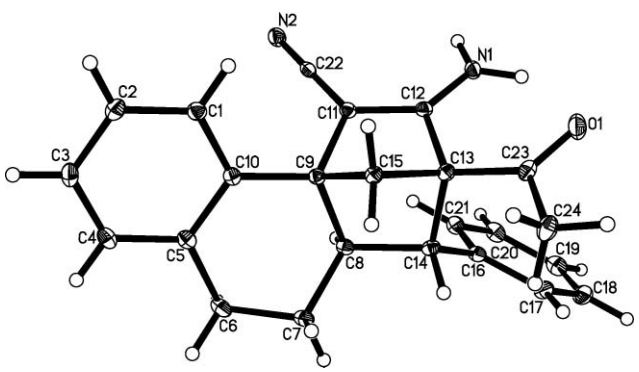


Fig. 1 X-Ray structure of racemic **2a**. Thermal ellipsoids are shown at 30% probability.

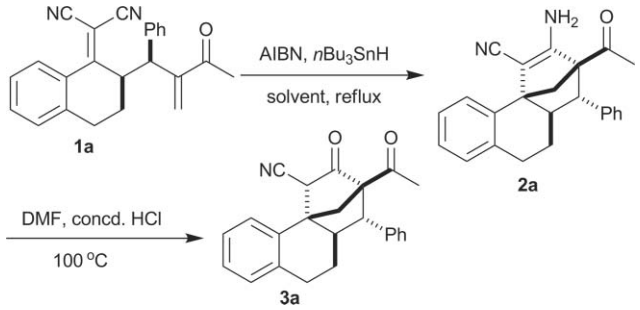
Nevertheless, much poorer results were obtained when toluene was used as the solvent (entry 2). In addition, enamine **2a** could

[a]*State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu, China*
[b]*Key Laboratory of Drug-Targeting and Drug Delivery System of Education Ministry, West China School of Pharmacy, Sichuan University, Chengdu, 610041, China. E-mail: ycchenhuaxi@yahoo.com.cn; Fax: 86 28 85502609; Tel: 86 28 85502609*

† Electronic supplementary information (ESI) available: NMR and HPLC spectra of the products, CIF file of racemic **2a**. CCDC reference number 763227. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c002378g

‡ Crystal data for racemic **2a** (CCDC 763227) $C_{24}H_{22}N_2O$ (354.44), monoclinic, space group $P2_1/c$, $a = 11.932(3)$, $b = 11.410(2)$, $c = 14.195(3)$ Å, $U = 1872.0(7)$ Å^3, $Z = 4$, specimen $0.43 \times 0.43 \times 0.43$ mm^3, $T = 93(2)$ K, Mac Scienc M18XHF22-SRA diffractometer, absorption coefficient 0.077 mm^{-1}, reflections collected/unique 14 779/4285 [R(int) = 0.0277], refinement by full-matrix least-squares on F^2, data/restraints/parameters 4285/0/253, goodness-of-fit on F^2 = 1.000, final R indices [$I > 2\sigma(I)$] $R_1 = 0.0423$, w$R_2 = 0.1019$, R indices (all data) $R_1 = 0.0542$, w$R_2 = 0.1092$, largest diff. peak and hole 0.311 and -0.273 e Å^{-3}.

Table 1 Screening studies of cyclisation reaction of allylic-allylic substrate **1a**[a]



Entry	Solvent	Time/h[b]	Yield (%)[c]
1	Benzene	1	**2a**, 66
2	Toluene	11	**2a**, 17
3[d]	Benzene	1	**3a**, 63
4[e]	Benzene	1	**3a**, 69

[a] Unless noted otherwise, reactions were conducted with 0.1 mmol of substrate **1a**, 0.3 mmol of nBu$_3$SnH, 0.03 mmol of AIBN in solvent (1 mL). [b] For radical cyclisation step. [c] Isolated yield. [d] After the completion of radical cyclisation, **2a** was isolated and heated in DMF/concd. HCl (1.2 mL, v/v = 2 : 1) overnight; yield for two steps. [e] After the completion of radical cyclisation, benzene was removed and the residue was directly heated in DMF/concd. HCl (1.2 mL, v/v = 2 : 1) overnight; yield for two steps.

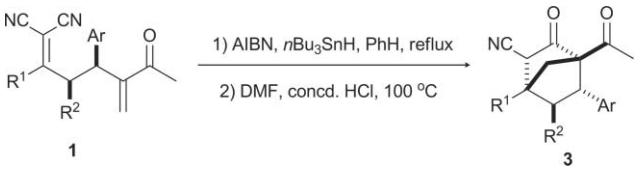
be easily hydrolysed to ketone **3a** under strong acidic conditions (entry 3). Moreover, a tandem cyclisation-hydrolysis reaction to **3a** could be more conveniently conducted in a one-pot procedure (entry 4).

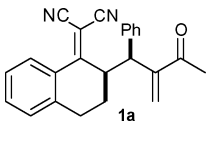
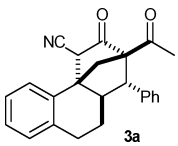
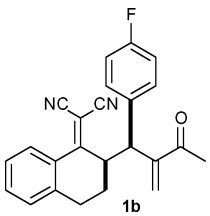
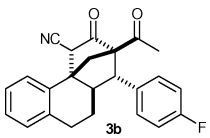
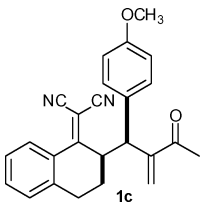
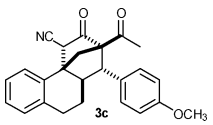
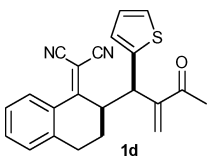
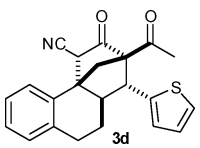
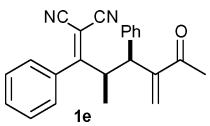
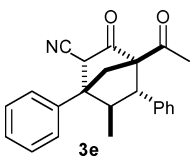
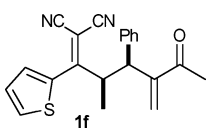
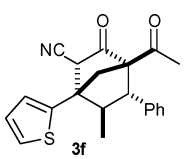
Consequently, a number of allylic substrates **1** were explored under the established conditions. A one-pot radical cyclization-hydrolysis process was performed to afford α-cyano ketones **3**. The results are summarised in Table 2. For substrates **1a–1d** derived from α,α-dicyanoalkene of α-tetralone (Table 2, entries 1–4), the tandem reaction proceeded smoothly, and the desired bridged cyclic products **3a–3d** were isolated in good yields and excellent diastereoselectivity, except for **3c** bearing an electron-donating aryl group (entry 3). More side reactions were observed for the reactions of acyclic allylic substrates **1e** and **1f**, while the bicyclic products **3e** and **3f** were isolated in fair yields and good diastereoselectivity (entries 5 and 6).

We have tested more allylic substrates **1g–1j** under the nBu$_3$SnH-mediated radical cyclisation conditions. Nevertheless, it was found that the tandem attack of the *O*-stannyl enolate to cyano group did not proceed. As illustrated in Table 3, the cyclopentane derivatives **4a–4d** were directly isolated in moderate yields but with excellent diastereoselectivity (dr > 95 : 5).

Since the highly enantioenriched allylic substrate **1** can be readily synthesised by modified cinchona alkaloid (DHQD)$_2$AQN-catalysed asymmetric allylic-allylic alkylation of α,α-dicyanoalkenes and Morita–Baylis–Hillman carbonates derived from MVK, we have prepared chiral allylic substrates **1a** and **1h**.[4a] As outlined in Scheme 2, the desired cyclic products *ent*-**3a** and *ent*-**4b** were efficiently delivered, respectively, with retained excellent enantiopurity under the established radical cyclisation conditions.

Table 2 One pot tandem cyclisation-hydrolysis to access bridged α-cyano ketone **3**[a]

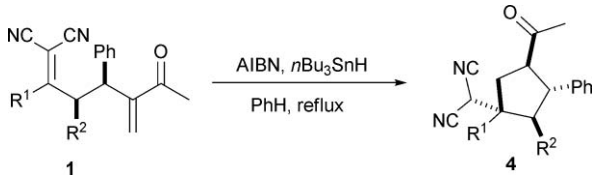


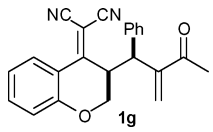
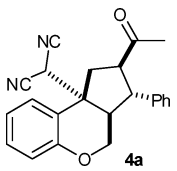
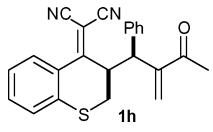
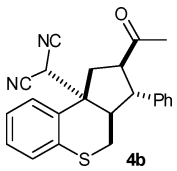
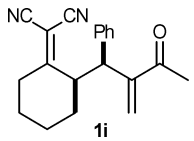
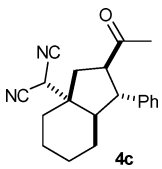
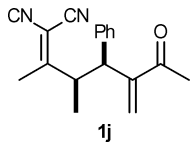
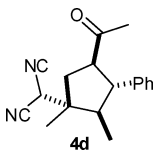
Entry	Substrate **1**	Product **3**	Yield (%)[b]	Dr[c]
1			69	>95 : 5
2			70	>95 : 5
3			69	67 : 33
4			69	>95 : 5
5			42	75 : 25
6			39	91 : 9

[a] Reactions were performed with 0.1 mmol of **1**, 0.3 mmol of nBu$_3$SnH, 0.03 mmol of AIBN in PhH (1.0 mL) for 1–12 h. After completion, benzene was removed, and the residue was stirred in a mixture of DMF/concd. HCl (1.2 mL, v/v = 2 : 1) at 100 °C overnight. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis.

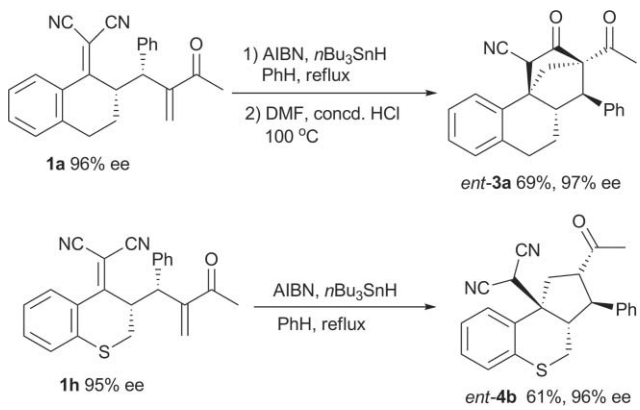
As outlined in Scheme 3, the plausible mechanism for the cyclisation reaction was proposed. As reported by Enholm *et al.*,[5] the allylic *O*-stannyl ketyl intermediate **A** would be generated from the reaction of α,β-unsaturated ketone **1** and nBu$_3$Sn radical. Subsequent intramolecular addition to activated C=C

Table 3 Cyclisation reaction to access cyclopentane derivative **4**[a]



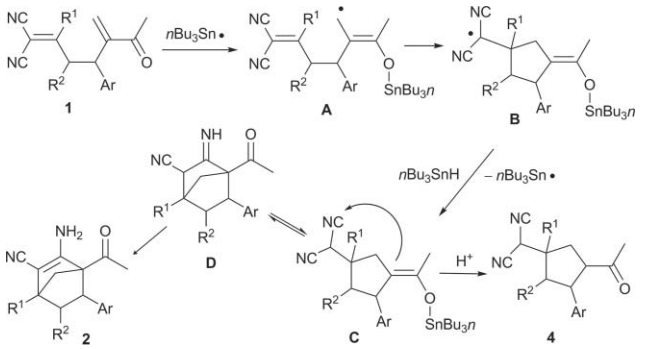
Entry	Substrate **1**	Product **4**	Yield (%)[b]
1			63
2			55
3			43
4			60

[a] Reactions were performed with 0.1 mmol of **1**, 0.3 mmol of nBu$_3$SnH, 0.03 mmol of AIBN in PhH (1 mL) for 2–6 h. [b] Isolated yield. Dr > 95 : 5, determined by ^{1}H NMR analysis.



Scheme 2 Radical cyclisation reactions of enantioenriched allylic substrates.

bond would occur to afford cyclopentane compound **B**. Transfer of a hydrogen radical from another nBu$_3$SnH would produce tin enolate **C** and give a molecule of nBu$_3$Sn radical to carry out the chain reaction. The nucleophilic tin enolate **C** could



Scheme 3 Proposed mechanism for the cascade cyclisation reaction.

attack electrophilic cyano group to give imine **D**, which would isomerise to more stable enamine product **2**. On the other hand, the *O*-stannyl enolate **C** might be directly hydrolysed to cyclopentane product **4** probably due to the structural instability of the formed bridged intermediate **D**.

Conclusions

We have investigated the intramolecular cyclisation reactions of multifunctional substrates which are readily available from the allylic-allylic alkylation of α,α-dicyanoalkenes and MBH carbonates of MVK. The reaction proceeded *via* an allylic *O*-stannyl ketyl intermediate, and two C–C bounds, two bridged rings and two quaternary carbon centres could be constructed in a domino process, which provided an efficient protocol to access cyclopentane derivatives with multiple substitutions in moderate to excellent diastereoselectivity. We hope that this methodology might be valuable for the synthesis of organic compounds with more molecular complexity.

Experimental

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, and ^{13}C NMR spectra were recorded at 50 or 100 MHz (Bruker Avance). Chemical shifts are reported in ppm downfield from $CDCl_3$ ($\delta = 7.27$ ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance ($\delta = 77.0$ ppm) for ^{13}C NMR spectroscopy. Coupling constants are given in Hz. Optical rotations were measured at 589 nm at 20 °C. Enantiomeric excess was determined by HPLC analysis on Chiralpak AD and Chiralcel OD columns. Benzene and toluene were distilled from CaH_2. All other chemicals were used without purification as commercially available. Racemic and chiral allylic substrates **1** were prepared according to the literature.[4a]

General one-pot procedure for the synthesis of bridged α-cyano ketone 3

Allylic substrate **1** (0.1 mmol), nBu$_3$SnH (88 mg, 0.3 mmol) and AIBN (5.0 mg, 0.03 mmol) in dry benzene (1.0 mL) were heated to reflux, and the reaction was monitored by TLC analysis. After

completion, the solvent was removed under reduced pressure (compound **2a** has been isolated and analysed), and the residue was stirred in a mixture of DMF/concd. HCl (1.2 mL, v/v = 2 : 1) at 100 °C overnight. The product was extracted by a mixture of ethyl acetate and petroleum ether (v/v = 1 : 1, 4 mL × 3) and washed with saturated sodium bicarbonate solution (5 mL) and brine (5 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated and the residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give α-cyano ketone **3**.

Compound 2a. 66% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.10 (m, 9H), 5.50 (s, 2H), 3.39 (d, J = 4.4 Hz, 1H), 2.97-2.82 (m, 2H), 2.52-2.49 (m, 1H), 2.48 (d, J = 9.2 Hz, 1H), 2.35-2.29 (m, 1H), 2.32 (s, 3H), 2.18 (dd, J = 1.6, 8.8 Hz, 1H), 1.75 (qd, J = 4.8, 12.8 Hz, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.4, 163.7, 137.6, 137.3, 134.7, 128.9, 128.4, 128.3, 127.8, 127.1, 126.6, 117.3, 68.2, 58.9, 56.7, 53.9, 50.0, 30.4, 30.3, 27.1 ppm; ESI-HRMS: calcd. for $C_{24}H_{22}N_2O$+H 355.1810, found 355.1819.

Compound 3a. 69% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.20 (m, 9H), 3.87 (s, 1H), 3.48 (d, J = 6.8 Hz, 1H), 2.95-2.79 (m, 2H), 2.70-2.64 (m, 1H), 2.62 (d, J = 11.6 Hz, 1H), 2.36 (dd, J = 1.6, 11.2 Hz, 1H), 2.25-2.20 (m, 1H), 1.99 (s, 3H), 1.68 (qd, J = 4.4, 12.8 Hz, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 203.2, 198.6, 138.7, 136.3, 132.7, 129.8, 128.9, 128.8, 128.2, 127.8, 127.0, 126.1, 114.8, 75.1, 58.7, 54.0, 48.7, 47.2, 44.9, 30.3, 29.9, 28.9 ppm; ESI-HRMS: calcd. for $C_{24}H_{21}NO_2$ + Na 378.1470, found 378.1490. *ent*-**3a** 69% yield; $[\alpha]_D^{20}$ = +31.1 (c = 0.75 in $CHCl_3$); 97% ee, determined by HPLC analysis [Daicel chiralpak AD, n-hexane/*i*-PrOH = 60/40, 1.0 mL min^{-1}, λ = 254 nm, t (major) = 9.5 min, t (minor) = 6.6 min].

Compound 3b. 70% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.20 (m, 6H), 7.07-7.02 (m, 2H), 3.88 (s, 1H), 3.53 (d, J = 6.8 Hz, 1H), 2.96-2.81 (m, 2H), 2.63-2.58 (m, 1H), 2.59 (d, J = 11.6 Hz, 1H), 2.38 (dd, J = 1.6, 11.2 Hz, 1H), 2.24-2.20 (m, 1H), 2.03 (s, 3H), 1.68 (qd, J = 4.0, 12.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.9, 198.7, 162.4 (d, $J_{C,F}$ = 246.2 Hz), 138.6, 132.4, 132.0 (d, $J_{C,F}$ = 3.2 Hz), 130.6 (d, $J_{C,F}$ = 8.2 Hz), 129.8, 127.9, 127.0, 126.1, 115.7 (d, $J_{C,F}$ = 21.3 Hz), 114.7, 74.9, 57.2, 54.0, 49.9, 47.3, 44.9, 30.2, 29.8, 28.8 ppm; ESI-HRMS: calcd. for $C_{24}H_{20}FNO_2$ + Na 396.1376, found 396.1401.

Compound 3c. 69% yield; dr = 67 : 33, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.09 (m, 6H), 6.92-6.85 (m, 2H), 3.86 (s, 1H), 3.80 (d, J = 6.4 Hz, 1H), 3.80 (s, 3H), 2.97-2.67 (m, 2H), 2.65-2.58 (m, 1H), 2.59 (d, J = 12.0 Hz, 1H), 2.34 (dd, J = 1.6, 11.6 Hz, 1H), 2.22-2.18 (m, 1H), 1.99 (s, 3H), 1.66 (qd, J = 4.4, 8.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.4, 198.7, 159.3, 138.6, 132.7, 130.0, 129.7, 128.5, 127.8, 126.9, 126.1, 114.5, 114.1, 75.1, 58.0, 55.2, 54.0, 50.8, 47.0, 44.9, 30.2, 28.8, 22.1 ppm; ESI-HRMS: calcd. for $C_{25}H_{23}NO_3$ + H 386.1756, found 386.1751.

Compound 3d. 69% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.19 (m, 5H), 7.01-6.96 (m, 2H), 3.87 (s, 1H), 3.86 (d, J = 7.2 Hz, 1H), 3.00-2.81 (m, 2H), 2.72-2.68 (m, 1H), 2.54 (d, J = 12.0 Hz, 1H), 2.39-2.31 (m, 2H), 2.18 (s, 3H), 1.70 (qd, J = 4.0, 12.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 193.4, 139.4, 138.5, 129.8, 127.9, 127.4, 127.0, 126.2, 126.0, 125.3, 114.4, 75.1, 53.7, 51.3, 50.1, 47.2, 46.7, 30.2, 29.7, 28.9, 28.6 ppm; ESI-HRMS: calcd. for $C_{22}H_{19}NO_2S$+Na 384.1034, found 384.1067.

Compound 3e. 42% yield; dr = 75 : 25, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45-7.22 (m, 10H), 3.48 (s, 1H), 3.32 (d, J = 6.8 Hz, 1H), 2.94-2.84 (m, 1H), 2.87 (d, J = 11.6 Hz, 1H), 2.37 (dd, J = 2.0, 11.2 Hz, 1H), 1.99 (s, 3H), 0.87 (d, J = 1.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.6, 198.4, 137.2, 136.3, 129.0, 128.8, 128.8, 128.2, 128.1, 126.5, 115.9, 74.2, 60.5, 53.7, 53.0, 42.6, 41.1, 19.2, 12.5 ppm; ESI-HRMS: calcd. for $C_{23}H_{21}NO_2$ + Na 366.1470, found 366.1468.

Compound 3f. 39% yield; dr = 91 : 9, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.22 (m, 6H), 7.06-7.04 (m, 1H), 7.02-6.99 (m, 1H), 3.38-3.32 (m, 1H), 3.08 (dd, J = 8.8, 11.2 Hz, 1H), 2.77 (s, 1H), 2.62 (dd, J = 5.6, 14.4 Hz, 1H), 2.52-2.47 (m, 1H), 2.04 (s, 3H), 0.91 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 211.8, 209.2, 149.2, 141.7, 128.9, 127.6, 127.2, 127.1, 124.1, 124.0, 118.4, 57.4, 54.7, 54.6, 49.4, 42.3, 30.2, 19.1, 12.2 ppm; ESI-HRMS: calcd. for $C_{21}H_{19}NO_2S$+Na 372.1034, found 372.1005.

General procedure for the synthesis of multiply substituted cyclopentanes 4

Allylic substrate **1** (0.1 mmol), nBu$_3$SnH (88 mg, 0.3 mmol) and AIBN (5.0 mg, 0.03 mmol) in dry benzene (1.0 mL) were refluxed under Ar, and monitored by TLC analysis. After completion, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give cyclopentane **4**.

Compound 4a. 63% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43-7.24 (m, 7H), 7.08-7.04 (m, 1H), 6.95-6.93 (m, 1H), 4.27 (s, 1H), 4.17 (dd, J = 2.8, 12.4 Hz, 1H), 3.95 (dd, J = 1.6, 12.4 Hz, 1H), 3.53-3.46 (m, 1H), 3.26 (t, J = 11.2 Hz, 1H), 2.73-2.67 (m, 2H), 2.61 (dd, J = 8.8, 14.0 Hz, 1H), 1.80 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.9, 153.6, 139.2, 129.9, 129.3, 128.0, 127.8, 127.2, 122.9, 122.7, 118.5, 112.1, 111.5, 62.3, 56.9, 51.1, 50.4, 44.8, 40.9, 35.3, 30.3 ppm; ESI-HRMS: calcd. for $C_{23}H_{20}N_2O_2$ + Na 379.1422, found 379.1431.

Compound 4b. 55% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56-7.54 (m, 1H), 7.41-7.25 (m, 8H), 4.30 (s, 1H), 3.78-3.71 (m, 1H), 3.04-2.93 (m, 4H), 2.75 (dd, J = 7.2, 14.0 Hz, 1H), 2.43-2.32 (m, 1H), 1.86 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 207.5, 139.0, 135.9, 135.1, 129.7, 129.7, 129.3, 128.6, 128.0, 127.5, 127.0, 112.9, 111.5, 56.6, 55.4, 55.0, 49.8, 38.9, 35.5, 30.9, 30.8 ppm; ESI-HRMS: calcd. for $C_{23}H_{20}N_2OS$+Na 395.1194, found 395.1159. *ent*-**4b** 61% yield; $[\alpha]_D^{20}$ = +12.2 (c = 1.1 in $CHCl_3$); 97% ee, determined by HPLC analysis [Daicel chiralcel OD, n-hexane/*i*-PrOH = 70/30, 1.0 mL min^{-1}, λ = 254 nm, t (major) = 13.1 min, t (minor) = 16.1 min.

Compound 4c. 43% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.24 (m, 5H), 4.09 (s, 1H), 3.48-3.43 (m, 1H), 3.32 (td, J = 5.6, 9.6 Hz, 1H),

2.39-2.33 (m, 2H), 2.11 (dd, $J = 5.6$, 14.0 Hz, 1H), 1.97 (s, 3H), 1.87-1.72 (m, 4H), 1.55-1.14 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 208.7$, 141.1, 129.0, 127.7, 127.4, 112.1, 111.8, 56.5, 49.6, 49.1, 45.8, 37.5, 30.4, 30.2, 30.0, 21.6, 21.0, 19.2 ppm; ESI-HRMS: calcd. for $C_{20}H_{22}N_2O$+Na 329.1630, found 329.1602.

Compound 4d. 60% yield; dr > 95 : 5, determined by ^{1}H NMR analysis; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.38$-7.24 (m, 5H), 3.66 (s, 1H), 3.32-3.26 (m, 1H), 2.89 (t, $J = 11.2$ Hz, 1H), 2.32-2.25 (m, 2H), 2.18 (dd, $J = 6.8$, 14.0 Hz, 1H), 1.90 (s, 3H), 1.27 (s, 3H), 0.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 208.4$, 140.6, 129.0, 127.6, 127.5, 112.0, 111.9, 56.6, 55.5, 49.2, 46.1, 38.9, 33.9, 30.5, 20.8, 12.0 ppm; ESI-HRMS: calcd. for $C_{18}H_{20}N_2O$+Na 303.1473, found 303.1446. *The relative configuration of* ***4d*** *has been established by NOE analysis.*

Acknowledgements

We are grateful for the financial support from PCSIRTC (IRT0846) and National Basic Research Program of China (973 Program) (2010CB833300).

Notes and references

1 For reviews, see: (*a*) D. Basavaiah, P. D. Rao and R. S. Hyma, *Tetrahedron*, 1996, **52**, 8001; (*b*) D. Basavaiah, A. J. Rao and T. Satyanarayana, *Chem. Rev.*, 2003, **103**, 811; (*c*) D. Basavaiah, K. V. Rao and R. J. Reddy, *Chem. Soc. Rev.*, 2007, **36**, 1581.

2 For reviews, see: (*a*) V. Singh and S. Batra, *Tetrahedron*, 2008, **64**, 4511; (*b*) S. Gowrisankar, H. S. Lee, H. S. Kim, K. Y. Lee and J. N. Kim, *Tetrahedron*, 2009, **65**, 8769.

3 (*a*) J. N. Kim, H. J. Lee and J. H. Gong, *Tetrahedron Lett.*, 2002, **43**, 9141; (*b*) C.-W. Cho and M. J. Krische, *Angew. Chem., Int. Ed.*, 2004, **43**, 6689; (*c*) C.-W. Cho, J.-R. Kong and M. J. Krische, *Org. Lett.*, 2004, **6**, 1337; (*d*) Y. Du, X. Han and X. Lu, *Tetrahedron Lett.*, 2004, **45**, 4967; (*e*) H. Park, C.-W. Cho and M. J. Krische, *J. Org. Chem.*, 2006, **71**, 7892; (*f*) D. J. V. C. van Steenis, T. Marcelli, M. Lutz, A. L. Spek, J. H. van Maarseveen and H. Hiemstra, *Adv. Synth. Catal.*, 2007, **349**, 281; (*g*) T.-Z. Zhang, L.-X. Dai and X.-L. Hou, *Tetrahedron: Asymmetry*, 2007, **18**, 1990; (*h*) Y.-Q. Jiang, Y.-L. Shi and M. Shi, *J. Am. Chem. Soc.*, 2008, **130**, 7202; (*i*) G.-N. Ma, S.-H. Cao and M. Shi, *Tetrahedron: Asymmetry*, 2009, **20**, 1086.

4 For studies from this group, see: (*a*) H.-L. Cui, J. Peng, X. Feng, W. Du, K. Jiang and Y.-C. Chen, *Chem.–Eur. J.*, 2009, **15**, 1574; (*b*) K. Jiang, J. Peng, H.-L. Cui and Y.-C. Chen, *Chem. Commun.*, 2009, 3955; (*c*) H.-L. Cui, X. Feng, J. Peng, K. Jiang and Y.-C. Chen, *Angew. Chem., Int. Ed.*, 2009, **48**, 5737; (*d*) X. Feng, Y.-Q. Yuan, H.-L. Cui, K. Jiang and Y.-C. Chen, *Org. Biomol. Chem.*, 2009, **7**, 3660; (*e*) S.-J. Zhang, H.-L. Cui, K. Jiang, R. Li, Z.-Y. Ding and Y.-C. Chen, *Eur. J. Org. Chem.*, 2009, 5804; (*f*) H.-L. Cui, J.-R. Huang, J. Lei, Z.-F. Wang, S. Chen, L. Wu and Y.-C. Chen, *Org. Lett.*, 2010, **12**, 720.

5 (*a*) E. J. Enholm and K. S. Kinter, *J. Am. Chem. Soc.*, 1991, **113**, 7784; (*b*) E. J. Enholm and K. S. Kinter, *J. Org. Chem.*, 1995, **60**, 4850.

6 (*a*) D. P. Curran, D. Kim, H.-T. Liu and W. Shen, *J. Am. Chem. Soc.*, 1988, **110**, 5900; (*b*) M. Giurg and J. Mlochowski, *Synth. Commun.*, 1999, **29**, 2281; (*c*) F. Beaugis, F. Dénès and P. Renaud, *Org. Lett.*, 2004, **6**, 2563; (*d*) B. Štefane, P. Brožič, M. Vehovc, T. L. Rižner and S. Gobec, *Eur. J. Med. Chem.*, 2009, **44**, 2563.

7 For an excellent review on the synthesis of cyclopentitols, see: V. B. Kurteva and C. A. M. Afonso, *Chem. Rev.*, 2009, **109**, 6809.

8 The diastereomeric ratio of >95 : 5 indicates that the minor isomer could not be detected by ^{1}H NMR analysis.

