Synthesis of a camphor-derived auxiliary and the application to the asymmetric Darzens reaction

Yamu Xia, Haixin Liu* and Xiaoli Dai

College of Chemical Engineering, Qingdao University of Science and Technology, Qingdao 266042, P. R. China

A readily available chiral camphor-derived auxiliary was synthesised through a highly efficient and short general route. The Darzens reaction of the auxiliary with aldehydes in the presence of base gave glycidic esters with almost complete diastereocontrol and high yield.

Keywords: Camphor-derived auxiliary, Darzens reaction, diastereoselectivity

Glycidic esters are very important synthetic intermediates because of their rich and useful functionality.[1–4] However, few methods exist for their synthesis in a concise and highly selective manner.[5–8] The most direct method to date is an asymmetric Darzens reaction[9] and good *ee*'s or *de*'s have been achieved by employing chiral auxiliaries or chiral reagents although in all of these processes two separate steps are required: an aldol-type reaction followed by ring closure.[10] Ghosh reported[11] the Darzens reaction using a chloroacetate derivative as a chiral auxiliary gave products in high stereoselectivity. The regioselective reaction of dichloromethyloxazoline with nitrobenzene under basic conditions using *t*-BuOK followed by trapping with carbonyl compounds, permitted a product to be obtained with high selectivity.[12] The aza-Darzens reaction of lithium diethyl iodomethylphosphonate with enantiopure N-(2,4,6-trimethylphenylsulfinyl)imines affords a single diastereomeric N-sulfinylaziridine 2-phosphonate which, on treatment with MeMgBr, gives the corresponding NH-aziridine 2-phosphonate chiral building blocks.[13]

Recently, the Darzens reaction using camphor derivatives as chiral auxiliaries has received general attention.[14,15] It has been discovered that amide stabilised sulfur ylides bearing a readily available chiral camphor-derived moiety react with aldehydes in the presence of base to give glycidic amides directly with complete diastereocontrol and almost complete control of enantioselectivity.[16] Bonner and Thornton established that a conformationally rigid camphor-derived N-propionyloxazolidinone effects asymmetric stereochemical control in *syn*-selective aldol condensations of the derived lithium and titanium enolates with a variety of aldehydes, and a product was synthesised with high stereoselectivity.[17] Palomo reported that (1*R*)-2-*endo*-bromoacetyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (*endo*-2-bromoacetylisoborneol) and it's trimethylsilyl ether are efficient reagents for the asymmetric Darzens reaction. From the *α,β*-epoxy ketone adducts the chiral inductor, camphor is removed, by treatment with ceric ammonium nitrate, to yield the corresponding epoxy acids which are isolated as their dicyclohexylammonium salts.[18]

The asymmetric Darzens reaction using a camphor derivative as a chiral auxiliary was studied through a series of experiments, and the control ability of the auxiliary in the Darzens reaction was tested. The chiral auxiliary was synthesised using camphor as starting material through a short general route. Finally, the reaction of the auxiliary with aldehydes in the presence of base gave glycidic esters with almost complete diastereocontrol and high yield.

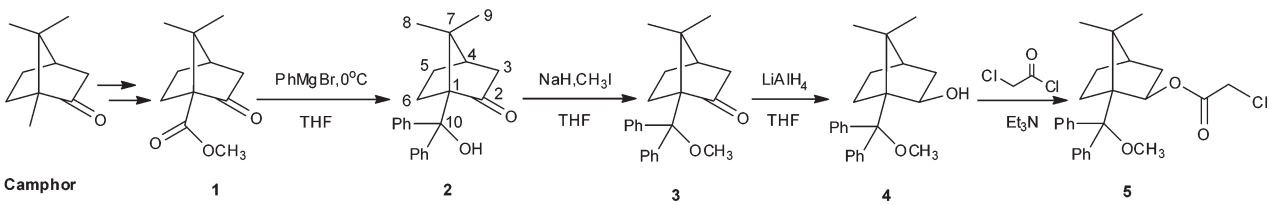
Results and discussion

Initially, we followed Bartlett's conditions using camphor as starting material through sulfonation, acylation and oxidation to afford compound **1**.[19] Subsequently, the Grignard reaction of compound **1** with PhMgBr gave compound **2**, and compound **2** was methylated with CH_3I in THF to give compound **3** and then reduction of **3** with $LiAlH_4$ gave compound **4** in high yield.[20] Ultimately, compound **5** was obtained through the reaction of compound **4** with chloroacetyl chloride (Scheme 1).

The Darzens reaction of compound **5** with aldehydes was studied through a series of experiments (Table 1).

As shown in Table 1, aldehydes 1, 7, 13, 19, 25 and 31 were chosen to react with compound **5**. CH_3CH_2ONa, NaH, *t*-BuOK and LDA were used to investigate the effect of the base, and only LDA had a better effect. Furthermore, the temperature plays an important role in the reaction. It should be pointed out that products were obtained with higher selectivity when the reaction was conducted at a lower temperature. Higher temperatures might speed up the reaction, but could lead to lower stereoselectivity and more by-products. When the reaction was conducted at −78 °C, the best result was achieved with a 99% level of selectivity with a 95% isolated yield (entry 16). Finally, the structure of aldehydes has an important impact on the reaction. The reaction rate of aldehydes with electron-donating groups is slower than aldehydes with a halogen group, but the stereoselectivity of the former is higher. However, we obtained products with high selectivity when we used aldehydes 1, 7, 13, 19, 25 and 31.

The compound **5** reacted with aldehydes *via* transition states **5B** and **5B'** to give glycidic esters with high diastereoselectivity. A proposed mechanism is shown in Scheme 2. This step involves the formation of an enol, which functions as a nucleophile. Compound **5** will react with LDA through a transition state which leads only to the (*E*)-enolate (**5A**). This enolate reacts with aldehydes through a six-membered chair-like transition state to afford glycidic esters with high selectivity. In the cyclic transition state, the avoidance of the destabilising 1,3-diaxial interactions is the controlling factor. Finally, a

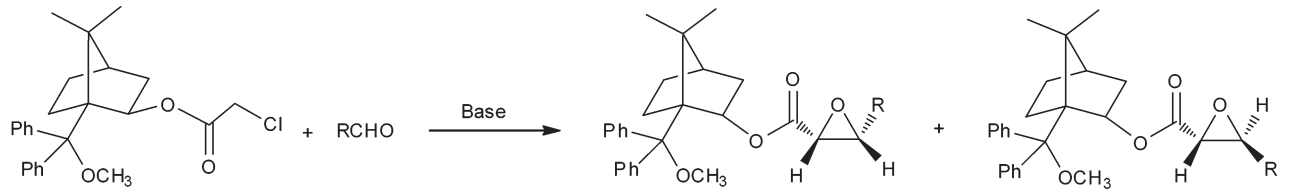


Scheme 1 Synthesis of compound **5**.

* Correspondent. E-mail: hdliuhaixin@126.com

Table 1 Effects of aldehydes, temperature, base and time on yield and structures of the products

Aldehyde	R	Temp./°C	Base	Time/h	Yield/%	Compound 6:7	Major, Minor product
1	Ph	–78	CH_3CH_2ONa	-	-	-	-
2		–78	NaH	-	-	-	-
3		–78	*t*-BuOK	-	-	-	-
4		–78	LDA	25	94	97:3	**6a**, **7a**
5		–40	LDA	16	85	94:6	**6a**, **7a**
6		–20	LDA	1.5	40	85:15	**6a**, **7a**
7	*o*-ClC_6H_4	–78	CH_3CH_2ONa	-	-	-	-
8		–78	NaH	-	-	-	-
9		–78	*t*-BuOK	-	-	-	-
10		–78	LDA	15	95	93:7	**6b**, **7b**
11		–40	LDA	10	86	89:11	**6b**, **7b**
12		–20	LDA	1	44	87:13	**6b**, **7b**
13	2-Thienyl	–78	CH_3CH_2ONa	-	-	-	-
14		–78	NaH	-	-	-	-
15		–78	*t*-BuOK	-	-	-	-
16		–78	LDA	35	95	>99:1	**6c**, -
17		–40	LDA	22	84	96:4	**6c**, -
18		–20	LDA	3	37	94:6	**6c**, -
19	4-Benzyloxy-3,5-dimethoxyphenyl	–78	CH_3CH_2ONa	-	-	-	-
20		–78	NaH	-	-	-	-
21		–78	*t*-BuOK	-	-	-	-
22		–78	LDA	30	93	98:2	**6d**, **7d**
23		–40	LDA	21	81	95:5	**6d**, **7d**
24		–20	LDA	2	37	87:13	**6d**, **7d**
25	Cinnamyl	–78	CH_3CH_2ONa	-	-	-	-
26		–78	NaH	-	-	-	-
27		–78	*t*-BuOK	-	-	-	-
28		–78	LDA	25	94	96:4	**6e**, **7e**
29		–40	LDA	17	82	93:7	**6e**, **7e**
30		–20	LDA	1.5	35	77:23	**6e**, **7e**
31	Pentyl	–78	CH_3CH_2ONa	-	-	-	-
32		–78	NaH	-	-	-	-
33		–78	*t*-BuOK	-	-	-	-
34		–78	LDA	27	94	97:3	**6f**, **7f**
35		–40	LDA	19	83	95:5	**6f**, **7f**
36		–20	LDA	1.5	42	86:14	**6f**, **7f**



5 **6 (*2R*, *3R*)** **7 (*2R*, *3S*)**

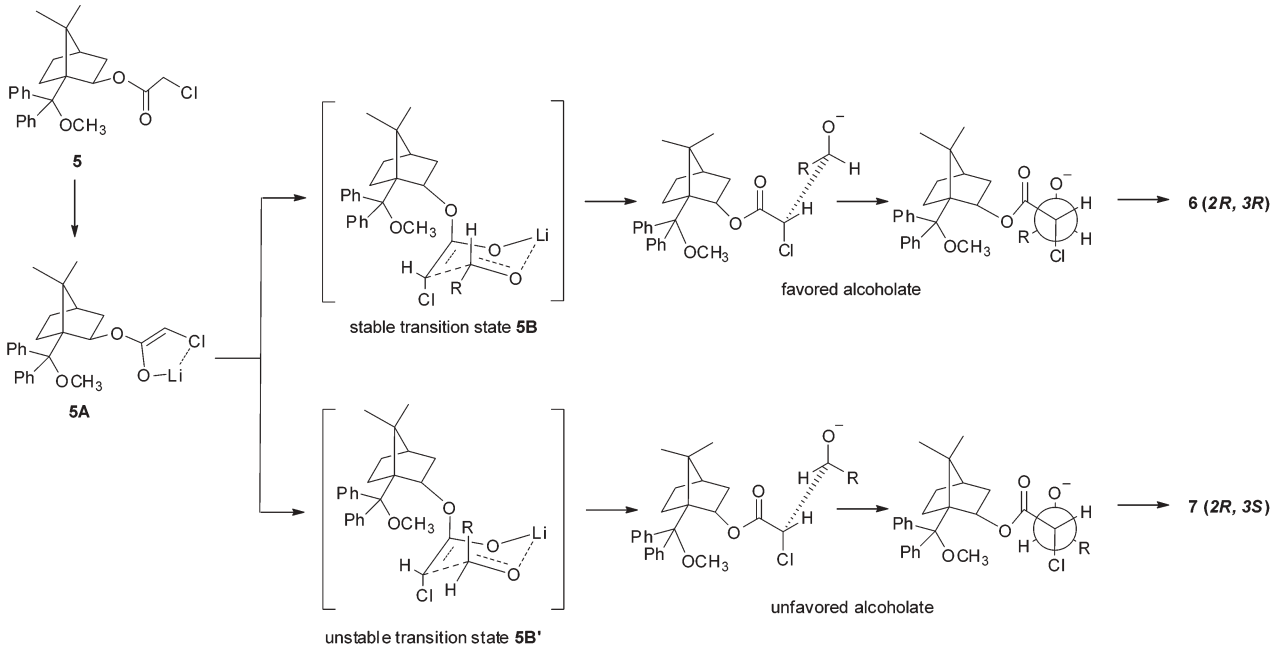
product was obtained with high selectivity (up to 99%) and high yield (up to 95%, entry 16, Table 1).

Experimental

All chemicals were used as supplied without further purification unless otherwise specified. Melting points were taken on a Gallenkamp melting point apparatus and were uncorrected. Optical rotations were determined on a Perkin-Elmer 341 polarimeter. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-500 MHz spectrometer. HRMS values were measured by a JEOL JMS-SX or JEOL JMS-SX 102A spectrometer. Flash column chromatography was performed on silica gel (200–300 mesh) (Qingdao Haiyang Chemical Co. Ltd, China) and TLC measurements were performed on silica gel GF254 plates (Qingdao Haiyang Chemical Co. Ltd, P.R. China).

Ketopinic acid methyl ester (**1**), *exo*-10,10-diphenyl-10-hydroxymethyl-7,7-dimethylbicyclo[2.2.1]heptane-2-one (**2**), *exo*-10,10-diphenyl-10-methoxymethyl-7,7-dimethylbicyclo[2.2.1]heptane-2-one (**3**) and *exo*-10,10-diphenyl-10-methoxymethyl-7,7-dimethylbicyclo-[2.2.1]heptane-2-ol (**4**) were synthesised according to the procedure which has been described previously.

exo-10,10-Diphenyl-10-methoxymethyl-7,7-dimethylbicyclo[2.2.1] heptyl-2-chloroacetate (**5**): A mixture of compound **4** (2.7 g, 8.04 mmol) and THF (50 mL) at 0 °C was added to a solution of chloroacetyl chloride (1.35 g, 11.9 mmol) in THF (30 mL). It was stirred for 20 min and triethylamine was added into the mixture. The reaction was put away from light until TLC revealed the absence of **4**. Then the reaction was quenched with $NaHCO_3$ aqueous solution, extracted with ethyl acetate, washed (brine), and dried over $MgSO_4$. Concentration *in vacuo* and flash column chromatography of the residue over silica gel gave compound **5** (3.0 g, 90.5%) as a white crystal. M.p. 265–268 °C, $[\alpha]_D^{20}$ = +18.6 (c = 0.2, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.78 (d, 2H, *J* = 7.5 Hz, ArH), 7.58 (d, 2H, *J* = 7.5 Hz, ArH), 7.40–7.26 (m, 6H, ArH), 4.90 (dd, 1H, *J* = 8.0, 3.5 Hz, CHOCO), 3.68 (d, 1H, *J* = 14.5, $COCH_aH_bCl$), 3.61 (d, 1H, *J* = 14.5, $COCH_aH_bCl$), 2.88–2.84 (m, 1H, CH), 2.83 (s, 3H, OCH_3), 1.88–1.19 and 0.99–0.96 (m, 6H, 3 × CH_2), 1.09 (s, 3H, CH_3), 0.61 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.9, 140.3, 138.5, 131.6, 129.5, 127.5, 127.3, 127.0, 126.8, 87.4, 82.5, 61.4, 52.7, 49.9, 49.1, 40.8, 39.0, 31.5, 25.5, 23.4, 22.5. HRMS *m/z* 412.1797 (calcd for $C_{25}H_{29}ClO_3$ 412.1805).



Scheme 2 A proposed mechanism for the synthesis of compound **6** and **7**.

General procedure for the preparation of **6** *and* **7**

6a and **7a**: A mixture of compound **5** (0.2 g, 0.48 mmol) and anhydrous THF (10 mL) was dropped into a solution of LDA (53.5 mmg, 0.5 mmol) in anhydrous THF (10 mL) at −78 °C under N_2, then benzaldehyde (0.08 mL, 0.75 mmol) was added, the mixture was stirred until TLC revealed the absence of benzaldehyde, the mixture was quenched with saturated NH_4Cl (5 mL), extracted with ethyl acetate, washed (saturated $NaHSO_3$ and NaCl), and dried over $MgSO_4$. Concentration *in vacuo* and flash column chromatography of the residue over silica gel (100 mL) using hexane/ethyl acetate (99:1) gave compound **6a** (0.18 g, 78%) as a pale yellow oil and then **7a** as a white oil. **6a**: $[\alpha]_D^{20}$ = +14.6 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.79–7.77 (m, 2H, ArH), 7.63–7.60 (m, 2H, ArH), 7.42–7.25 (m, 8H, ArH), 7.13–7.11 (m, 3H, ArH), 4.96 (dd, 1H, *J* = 8.5, 3.5 Hz, CHOCO), 3.72 (d, 1H, *J* = 2.0 Hz, OCHAr), 3.18 (d, 1H, *J* = 2.0 Hz, OCOCH), 2.99–2.97 (m, 1H, CH), 2.75 (s, 3H, OCH_3), 1.91–1.38 and 1.05–0.97 (m, 6H, 3 × CH_2), 1.08 (s, 3H, CH_3), 0.43 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.8, 140.3, 138.0, 135.0, 131.7, 129.7, 129.1, 128.7, 127.5, 127.2, 126.8, 126.6, 125.9, 87.1, 82.1, 61.6, 57.7, 56.8, 52.6, 49.6, 49.1, 39.2, 31.3, 25.7, 22.8, 22.0. HRMS *m/z* 482.2448 (calcd for $C_{32}H_{34}O_4$ 482.2457). **7a**: $[\alpha]_D^{20}$ = +18.3 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.82–7.79 (m, 2H, ArH), 7.62–7.59 (m, 2H, ArH), 7.43–7.26 (m, 8H, ArH), 7.14–7.12 (m, 3H, ArH), 4.97 (dd, 1H, *J* = 8.5, 3.5 Hz, CHOCO), 3.59 (d, 1H, *J* = 2.0 Hz, OCHAr), 3.08 (d, 1H, *J* = 2.0 Hz, OCOCH), 3.01–2.99 (m, 1H, CH), 2.79 (s, 3H, OCH_3), 1.93–1.39 and 1.06–0.98 (m, 6H, 3 × CH_2), 1.09 (s, 3H, CH_3), 0.60 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ:166.9, 140.3, 138.1, 135.1, 131.9, 129.9, 129.2, 128.8, 127.5, 127.2, 126.9, 126.6, 125.9, 86.9, 82.3, 61.0, 57.8, 56.9, 52.8, 49.7, 49.2, 39.2, 31.3, 25.8, 22.9, 22.0. HRMS *m/z* 482.2450 (calcd for $C_{32}H_{34}O_4$ 482.2457).

All the other products are given by analogy (**6b** and **7b**; **6c**; **6d** and **7d**; **6e** and **7e**; **6f** and **7f**).

6b and **7b**. **6b**: $[\alpha]_D^{20}$ = −48.5 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85–7.79 (m, 2H, ArH), 7.71–7.68 (m, 2H, ArH), 7.43–7.02 (m, 10H, ArH), 4.89–4.85 (m, 1H, CHOCO), 4.04 (d, 1H, *J* = 1.5 Hz, CHC*H*C), 3.95 (d, 1H, *J* = 1.5 Hz, OCOCH), 2.90–2.83 (m, 1H, CH), 2.81 (s, 3H, OCH_3), 1.66–1.41 and 1.11–1.01 (m, 6H, 3 × CH_2), 1.11 (s, 3H, CH_3), 0.79 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.6, 140.1, 139.8, 138.8, 133.5, 133.3, 131.5, 129.7, 129.6, 129.2, 128.7, 127.5, 127.4, 127.0, 126.8, 87.6, 82.4, 61.1, 56.3, 55.8, 55.2, 52.6, 50.1, 48.9, 39.2, 31.2, 23.3, 22.7. HRMS *m/z* 516.2075 (calcd for $C_{32}H_{33}ClO_4$ 516.2067). **7b**: $[\alpha]_D^{20}$ = +26.5 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.87–7.81 (m, 2H, ArH), 7.73–7.70 (m, 2H, ArH), 7.44–7.04 (m, 10H, ArH), 4.92–4.89 (m, 1H, CHOCO), 4.04 (d, 1H, *J* = 1.5 Hz, CHC*H*C), 3.94 (d, 1H, *J* = 1.5 Hz, OCOCH), 2.89–2.82 (m, 1H, CH), 2.83 (s, 3H, OCH_3), 1.67–1.42 and 1.13–1.03 (m, 6H, 3 × CH_2), 1.13 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.8, 140.7, 140.1, 139.0, 133.8, 133.6, 131.6, 129.9, 129.8, 129.3, 128.7, 127.6, 127.5, 127.1, 126.7, 87.7, 82.6, 61.5, 56.7, 55.8, 55.3, 52.7, 50.2, 49.1, 39.5, 31.3, 23.4, 22.8. HRMS *m/z* 516.2076 (calcd for $C_{32}H_{33}ClO_4$ 516.2067).

6c: $[\alpha]_D^{20}$ = +15.6 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.78–7.76 (m, 2H, ArH), 7.50–7.19 (m, 9H, ArH), 7.19 (d, 1H, *J* = 3.5 Hz, CHC*H*=CH), 7.07 (dd, 1H, *J* = 5.0, 4.0 Hz, C=C*H*CH=CH), 6.29 (d, 1H, *J* = 2.0 Hz, COCH), 5.82 (d, 1H, *J* = 2.0 Hz, OCOCH), 4.84 (dd, 1H, *J* = 8.0, 3.0 Hz, CHOCO), 2.82 (s, 3H, OCH_3), 2.70–2.55 (m, 1H, CH), 1.81–1.54 and 0.90–0.64 (m, 6H, 3 × CH_2), 1.27 (s, 3H, CH_3), 1.17 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ:164.2, 139.3, 139.2, 137.5, 136.9, 131.3, 129.7, 129.1, 128.1, 127.4, 127.3, 127.1, 126.9, 105.9, 88.5, 82.8, 60.8, 53.1, 52.6, 50.7, 48.9, 39.0, 31.3, 25.1, 23.7, 23.6. HRMS *m/z* 488.2012 (calcd for $C_{30}H_{32}O_4S$ 488.2021).

6d and **7d**. **6d**: $[\alpha]_D^{20}$ = +68.1 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85 (d, 2H, *J* = 8.0 Hz, ArH), 7.59 (d, 2H, J = 8.0 Hz, ArH), 7.49–7.41 (m, 3H, ArH), 7.36–7.11 (m, 8H, ArH), 6.40 (s, 2H, ArH), 5.00 (s, 2H, $ArCH_2$), 4.99–4.97 (m, 1H, CHOCO), 3.84 (s, 6H, 2 × OCH_3), 3.47 (d, 1H, *J* = 1.5 Hz, OCHAr), 3.04 (d, 1H, *J* = 2.0 Hz, OCOCH), 2.91–2.85 (m, 1H, CH), 2.78 (s, 3H, $ArCOCH_3$), 1.93–1.15 and 1.01–0.95 (m, 6H, 3 × CH_2), 1.09 (s, 3H, CH_3), 0.61 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.1, 153.8, 140.6, 138.9, 138.3, 137.5, 137.2, 131.6, 130.7, 129.9, 128.5, 128.2, 128.0, 127.6, 127.1, 126.9, 126.6, 106.6, 102.5, 87.4, 82.6, 75.1, 61.3, 57.2, 56.8, 56.2, 56.1, 52.5, 49.8, 49.2, 39.4, 31.7, 25.6, 23.5, 22.5. HRMS *m/z* 648.3096 (calcd for $C_{41}H_{44}O_7$ 648.3087). **7d**: $[\alpha]_D^{20}$ = −52.6 (c = 0.005, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.82 (d, 2H, *J* = 8.0 Hz, ArH), 7.61 (d, 2H, *J* = 8.0 Hz, ArH), 7.51–7.43 (m, 3H, ArH), 7.35–7.10 (m, 8H, ArH), 6.47 (s, 2H, ArH), 5.04 (s, 2H, $ArCH_2$), 4.97–4.95 (m, 1H, CHOCO), 3.83 (s, 6H, 2 × OCH_3), 3.69 (d, 1H, *J* = 1.5 Hz, OCHAr), 3.12 (d, 1H, *J* = 2.0 Hz, OCOCH), 2.93–2.87 (m, 1H, CH), 2.77 (s, 3H, $ArCOCH_3$), 1.96–1.16 and 1.03–0.97 (m, 6H, 3 × CH_2), 1.06 (s, 3H, CH_3), 0.42 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ:167.0, 153.9 140.5, 138.8, 138.2, 137.4, 137.1, 131.7, 130.7, 130.0, 128.4, 128.1, 127.9, 127.7, 127.2, 127.0, 126.8, 106.5, 102.5, 87.4, 82.4, 75.1, 61.4, 57.2, 56.8, 56.2, 56.1, 53.5, 49.6, 49.1, 39.3, 31.3, 25.7, 23.6, 22.6. HRMS *m/z* 648.3092 (calcd for $C_{41}H_{44}O_7$ 648.3087).

6e and **7e**. **6e**: $[\alpha]_D^{20}$ = −21.8 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85–7.75 (m, 4H, ArH), 7.57–7.23 (m, 11H, ArH), 6.80 (d, 1H, *J* = 5Hz, CH=C*H*Ar), 6.58 (d, 1H, *J* = 5.0 Hz, C*H*=CHAr), 4.90–4.89 (m, 1H, C*H*OCO), 3.64 (d, 1H, *J* = 1.5 Hz, C*H*CH=CH), 3.42 (d, 1H, *J* = 2 Hz, OCOCH), 2.90–2.83 (m, 1H, CH), 2.80 (s, 3H, OCH_3), 1.86–1.16 and 0.96–0.94 (m, 6H, 3 × CH_2), 1.08 (s, 3H, CH_3), 0.59 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.5, 140.2, 139.5, 136.7, 131.5, 130.7, 129.7, 129.4, 128.9, 128.6, 127.4, 126.9, 126.7, 123.0, 86.9, 82.7, 62.5, 52.6, 49.8, 49.0, 40.5, 39.6, 31.4, 29.6, 25.4, 23.3, 22.4, 14.9. HRMS *m/z* 508.2619 (calcd for $C_{34}H_{36}O_4$ 508.2614).

7e: $[\alpha]_D^{20}$ = +30.4 (c = 0.005, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.86–7.76 (m, 4H, ArH), 7.57–7.23 (m, 11H, ArH), 6.90 (d, 1H, *J* = 5Hz, CH=C*H*Ar), 6.46 (d, 1H, *J* = 5Hz, C*H*=CHAr), 4.87–4.85 (m, 1H, C*H*OCO), 3.65 (d, 1H, *J* = 1.5 Hz, C*H*CH=CH), 3.43 (d, 1H, *J* = 2 Hz, OCOCH), 2.91–2.84 (m, 1H, CH), 2.81 (s, 3H, OCH_3), 1.87–1.16 and 0.96–0.94 (m, 6H, 3 × CH_2), 1.09 (s, 3H, CH_3), 0.61 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.4, 140.3, 139.6, 136.8, 131.6, 130.9, 129.7, 129.5, 128.8, 128.5, 127.6, 127.1, 126.9, 123.2, 87.1, 82.9, 62.7, 53.0, 49.9, 49.2, 40.8, 39.8, 31.6, 29.9, 25.7, 23.4, 22.5, 14.8. HRMS *m*/*z* 508.2623 (calcd for $C_{34}H_{36}O_4$ 508.2614).

6f and **7f**. **6f**: $[\alpha]_D^{20}$ = +52.3 (c = 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.93 (d, 2H, *J* = 10 Hz, ArH), 7.68 (d, 2H, *J* = 10 Hz, ArH), 7.42–7.26 (m, 6H, ArH), 4.92–4.91 (m, 1H, C*H*OCO), 3.12–3.02 (m, 1H, CH), 2.96 (d, 1H, *J* = 1.5 Hz, OC*H*CH_2), 2.82 (d, 1H, *J* = 2.0 Hz, OCOCH), 2.80 (s, 3H, CH_3), 1.96–1.57, 1.53–1.46 and 0.98–0.87 (m, 6H, 3 × CH_2), 1.57–1.54 (m, 2H, OCHCH_2CH_2), 1.44–1.37 (m, 2H, $CH_2CH_2CH_3$), 1.34–1.28 (m, 2H, $CH_2CH_2CH_2$), 1.06 (s, 3H, CH_3), 0.99 (s, 3H, CH_2CH_3), 0.37 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.8, 140.4, 138.3, 131.9, 129.7, 127.4, 127.2, 126.8, 126.6, 86.9, 82.0, 61.6, 58.1, 53.0, 52.6, 49.4, 49.1, 39.2, 31.2, 31.1, 27.8, 25.8, 22.8, 22.4, 21.7, 13.9. HRMS *m*/*z* 462.2764 (calcd for $C_{30}H_{38}O_4$ 462.2770). **7f**: $[\alpha]_D^{20}$ = +55.6 (c = 0.005, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.87 (d, 2H, *J* = 10 Hz, ArH), 7.61 (d, 2H, *J* = 10 Hz, ArH), 7.41–7.25 (m, 6H, ArH), 4.91–4.90 (m, 1H, C*H*OCO), 3.11–3.01 (m, 1H, CH), 2.94 (d, 1H, *J* = 1.5 Hz, OC*H*CH_2), 2.81 (d, 1H, *J* = 2.0 Hz, OCOCH), 2.80 (s, 3H, CH_3), 1.97–1.58, 1.54–1.47 and 0.97–0.86 (m, 6H, 3 × CH_2), 1.58–1.55 (m, 2H, OCHCH_2CH_2), 1.45–1.38 (m, 2H, $CH_2CH_2CH_3$), 1.35–1.29 (m, 2H, $CH_2CH_2CH_2$), 1.10 (s, 3H, CH_3), 1.01 (s, 3H, CH_2CH_3), 0.38 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.6, 140.5, 138.9, 131.5, 129.6, 127.5, 127.1, 126.9, 126.6, 87.8, 82.4, 61.4, 57.7, 53.0, 52.7, 49.5, 49.0, 39.3, 31.3, 31.2, 28.4, 26.9, 22.9, 22.5, 21.8, 14.0. HRMS *m*/*z* 462.2761 (calcd for $C_{30}H_{38}O_4$ 462.2770).

This work was supported by the National Natural Science Foundation of Shandong (No. ZR2010HM023), the Chinese Medicine Administration Bureau of Gansu Province (No. GZK-2011-62).

Received 20 May 2013; accepted 18 June 2013
Paper 1201912 doi: 10.3184/174751913X13737254410429
Published online: 6 September 2013

References

1 G. Lemonnier, L. Zoute, J.C. Quirion and P. Jubault, *Org. Lett.*, 2010, **12**, 844.
2 M. Curini, F. Epifano, M.C. Marcotullio and O. Rosati, *Eur. J. Org. Chem.*, 2002, **9**, 1562.
3 M.V. Reddy, S.V. Pitre, I. Bhattacharya and Y.D. Vankar, *Synlett.*, 1996, **3**, 241.
4 M. Mamaghani, K. Tabatabaeian, A. Ghanadzadeh and F. Habibi, *Tetrahedron Lett.*, 2003, **44**, 4775.
5 E.N. Jacobsen, L. Deng, Y. Furukawa and L.E. Martinez, *Tetrahedron*, 1994, **50**, 4323.
6 M.J. Porter and J. Skidmore, *Chem. Commun.*, 2000, 1215.
7 O.M. Cohn, D. Williams and Y. Chen, *Chem. Commun.*, 2000, 495.
8 T. Nemoto, T. Ohshima and M. Shibasaki, *J. Am. Chem. Soc.*, 2001, **123**, 9474.
9 T. Rosen, B.M. Trost, I. Fleming and C.H. Heathcock, *Compr. Org. Synth.*, 1991, **2**, 409.
10 S. Arai, T. Suzuki, K. Tokumaru and T. Shioiri, *Tetrahedron Lett*., 2002, **43**, 833.
11 A.K. Ghosh and J.H. Kim, *Org. Lett.*, 2004, **6**, 2725.
12 S. Florio, P. Lorusso, C. Granito, R. Luisi and L. Troisi, *J. Org. Chem.*, 2004, **69**, 4961.
13 F.A. Davis, T. Ramachandar and Y. Wu, *J. Org. Chem.*, 2003, **68**, 6894.
14 Y. Cheng, H. Wu, P. Wu, Y. Shen and B. Uang, *Chem-Asian J.*, 2012, **7**, 2921.
15 J. Weng, H.B. Ai, R.S. Luo and G. Lu, *Chirality*, 2012, **24**, 271.
16 V.K. Aggarwal, G. Hynd, W. Picoul and J.L. Vasse, *J. Am. Chem. Soc.*, 2002, **124**, 9964.
17 M.P. Bonner and E.R. Thornton, *J. Am. Chem. Soc*., 1991, **113**, 1299.
18 C. Palomo, M. Oiarbide, A.K. Sharma, M.C. Gonzalez, A. Linden, J.M. Garcia and A. Gonzalez, *J. Org. Chem.*, 2000, **65**, 9007.
19 P.D. Bartlett and L.H. Knox, *Org. Synth.*, 1973, **5**, 689.
20 Y.Y. Chu, C.S. Yu, C.J. Chen, K.S. Yang, J.C. Lain, C.H. Lin and K. Chen, *J. Org. Chem.*, 1999, **64**, 6993.