First Stereoselective and Concise Synthesis of Rhoiptelol C

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The first concise stereoselective total synthesis of diarylheptanoid rhoiptelol C (**1**) was achieved from readily available vanillin. The synthesis involves *Keck*'s asymmetric allylation, olefin cross metathesis, and *Sharpless* asymmetric dihydroxylation reaction as key steps.

Introduction. – Diarylheptanoids are an important class of structurally distinct plant natural metabolites containing the 1,7-diphenylheptane moiety. More than 400 diarylheptanoids have been isolated from plant sources since the first diarylheptanoid was identified in 1815. These are mainly divided into three major groups: linear, cyclic biphenyls ([7.0]metacyclophanes), and cyclic diphenyl ethers ([7.1]metaparacyclophanes) on the basis of their structures [1]. The diarylheptanoids are mainly isolated from *Zingiber*, *Curcuma*, *Alpinia*, *Viscum*, *Alnus*, and *Myrica* species, and they exhibit a broad range of biological and pharmacological properties. Especially, linear diarylheptanoids exhibhit antiplatelet, anti-inflammatory, antioxidant, antiproliferative, antiemetic, cytotoxic, and prostaglandin E_2-inhibitory activities [2]. Rhoiptelol C (**1**; *Fig.*), a linear diarylheptanoid, was first isolated in 1996 by *Jiang et al.* from the fruits of *Rhoiptelea chiliantha,* along with two other diarylheptanoids. It was also isolated from the stems of *Engelhardia roxburghiana* in 2012 by *Wu et al*. [3]. The structure of **1** was elucidated on the basis of its spectroscopic data.

Due to the interesting structure of **1** with three contiguous stereogenic C-atoms bearing OH groups and in continuation of our work on syntheses of bioactive natural diarylheptanoids [4], we became interested in the synthesis of **1** in a simple and concise manner. Here, we report an efficient approach to the stereoselective synthesis of **1** employing *Keck*'s asymmetric allylation, olefin cross metathesis, and *Sharpless* asymmetric dihydroxylation reaction as key steps.

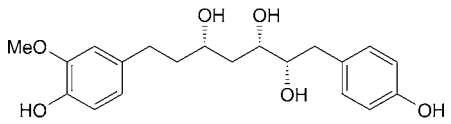

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Figure. *Structure of rhoiptelol C* (**1**)

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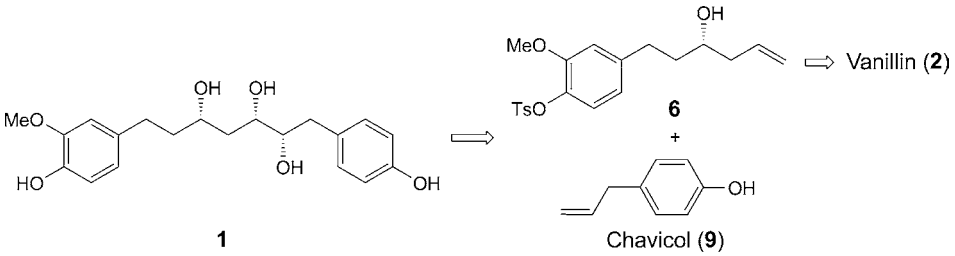
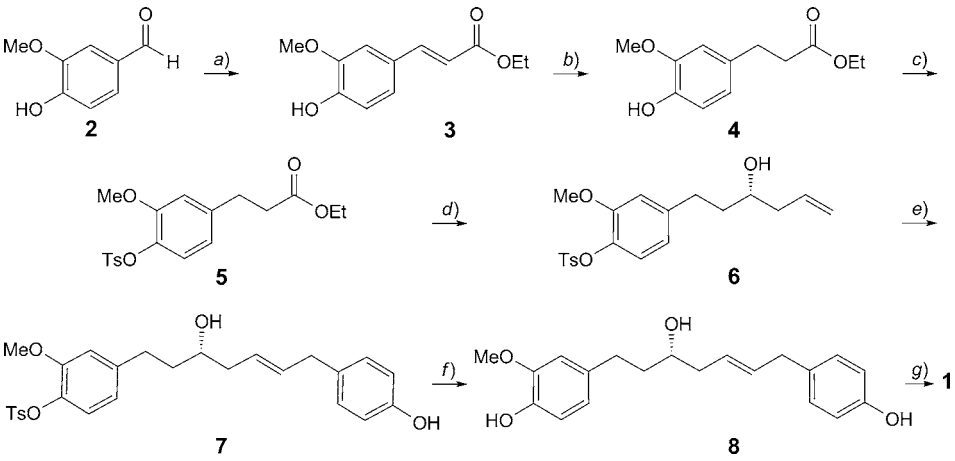
Scheme 1. *Retrosynthetic Analysis*



The retrosynthetic analysis of **1** is depicted in *Scheme 1*. The target molecule **1** can be easily envisaged from the olefin cross metathesis of compound **6** and chavicol (=4-(prop-2-en-1-yl)phenol; **9**). Compound **6** was prepared *via Keck*'s asymmetric allylation of an aldehyde derived from the reduction of the corresponding ester. The latter was prepared from vanillin (**2**) by *Wittig* olefination, followed by the reduction of the α,β-unsaturated C=C bond.

Results and Discussion. – As outlined in *Scheme 2*, the synthesis of **1** started with the aldehyde **2** and C_2-*Wittig* olefination with [(ethoxycarbonyl)methylidene]triphenylphosphane (Ph_3P=CHCOOEt) to furnish the α,β-unsaturated ester **3** in 96% yield (mixture of (*E*)- and (*Z*)-isomers) [5]. The C=C bond in **3** was reduced with $NiCl_2 \cdot 6\,H_2O/NaBH_4$ in MeOH to afford the saturated ester **4** [6] in 93% yield. The phenolic OH group in **4** was protected as Ts ester **5** in 91% yield by treatment with TsCl

Scheme 2.



a) Ph_3P=CHCOOEt, benzene, reflux, 1 h; 96%. *b*) $NiCl_2 \cdot 6\,H_2O$, $NaBH_4$, MeOH, 0° to r.t., 1 h; 93%. *c*) TsCl, Et_3N, CH_2Cl_2, 0° to r.t., 2 h; 91%. *d*) 1. Diisobutylaluminium hydride (DIBAL-H), CH_2Cl_2, −78°, 0.5 h; 92%. 2. (*R*)-[1,1′-Binapthalene]-2,2′-diol ((*R*)-BINOL), 4-Å molecular sieves (MS), $Ti(O^iPr)_4$, allyl(tributyl)stannane, dry CH_2Cl_2, −78° to −20°, 24 h; 89%. *e*) Chavicol, *Grubbs*' 2nd-generation catalyst (5 mol-%), dry CH_2Cl_2, 40°, 2 h; 81%. *f*) K_2CO_3, MeOH, reflux, 2 h; 80%. *g*) *AD-mix-α*, ^{t}BuOH/H_2O 1:1, $MeSO_2NH_2$, 24 h, 0°; 75%.

and Et_3N. Further, the ester **5** was reduced with DIBAL-H in dry CH_2Cl_2 to furnish the corresponding aldehyde, which was subjected to the *Keck*'s asymmetric allylation [7] with allyl(tributyl)stannane in the presence of the Ti complex of (*R*)-BINOL to furnish the chiral allylic alcohol **6** in 89% yield (enantiomeric excess 96%, determined by chiral HPLC). The cross metathesis of **6** with commercially available chavicol (**9**) (1:5) in the presence of *Grubbs*' second-generation catalyst afforded **7** in 81% yield (as a mixture of (*E*)- and (*Z*)-isomers in a 9:1 ratio, which were separable by SiO_2 column chromatography [8]). The Ts group in **7** was removed with K_2CO_3 in MeOH to give **8** in 81% yield. Finally, **8** was subjected to *Sharpless* asymmetric dihydroxylation [9] using *AD-mix-α* to provide the desired rhoiptelol C (**1**) in 75% yield. The physical and spectroscopic properties of **1** were in complete agreement with those reported in [3].

In conclusion, the first concise stereoselective synthesis of the natural product rhoiptelol C (**1**) was accomplished in seven steps in 32% overall yield the from commercially available starting material vanillin (**2**) by applying *Keck*'s asymmetric allylation, *Grubbs*' olefin cross-metathesis reaction, and *Sharpless* asymmetric dihydroxylation as the key steps.

The authors *S. P. R.* and *B. C.* are grateful to *UGC-CSIR*, New Delhi, India, for financial support in the form of fellowship.

Experimental Part

General. All the reagents and solvents were of reagent grade and used without further purification unless otherwise stated. Technical-grade AcOEt and hexanes used for column chromatography were distilled before use. THF, when used as solvent for the reactions, was freshly distilled from Na/benzophenone ketyl. All the reactions were performed under N_2 in flame- or oven-dried glassware with magnetic stirring. Column chromatography (CC): silica gel (SiO_2; 60–120 mesh) packed in glass columns. Optical rotations: *Anton Paar MLP 200* modular circular digital polarimeter by using a 2-ml cell with a path length of 1 dm. FT-IR Spectra: *Perkin-Elmer 683* IR spectrophotometer; neat or as thin films in KBr optics; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker-Avance 300* instrument (at 300 and 75 MHz, resp.) at r.t.; in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *Agilent Technologies LC-MSD* trap SL spectrometer; in *m*/*z*.

*Ethyl (2*E*)-3-(4-Hydroxy-3-methoxyphenyl)prop-2-enoate* (**3**) [5a]. To a soln. of *vanillin* (**2**; 4 g, 26.28 mmol) in benzene (40 ml) was added $Ph_3P{=}CHCOOEt$ (10.97 g, 31.54 mmol), and the mixture was stirred at reflux for 1 h. After completion of the reaction, the mixture was diluted with H_2O and extracted with AcOEt, the solvent was removed under reduced pressure, and the residue was purified by CC (AcOEt/hexane 95:5) to afford **3** (5.60 g, 96%) as an (*E*/*Z*)-mixture. Colorless syrup. IR (neat): 3421, 1712, 1638, 1223, 1132. ^1H-NMR (300 MHz, $CDCl_3$): 7.62 (*d*, *J* = 15.8, 1 H); 7.12–7.01 (*m*, 2 H); 6.92 (*d*, *J* = 8.1, 1 H); 6.29 (*d*, *J* = 15.8, 1 H); 4.26 (*q*, *J* = 7.1, 2 H); 3.92 (*s*, 3 H); 1.34 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 167.2; 147.9; 146.7; 144.6; 126.9; 122.9; 115.4; 114.7; 109.3; 60.2; 55.8; 14.2. ESI-MS: 245 (100, $[M + Na]^+$).

Ethyl 3-(4-Hydroxy-3-methoxyphenyl)propanoate (**4**) [6]. To a stirred soln. of **3** (5 g, 22.52 mmol) in MeOH (100 ml), $NiCl_4 \cdot 6\,H_2O$ (1.06 g, 4.50 mmol) was added at 0°. The resulting mixture was stirred at 0° for 10 min, and $NaBH_4$ (1.71 g, 45.04 mmol) was added in small portions. The mixture was stirred for another h, and the reaction was quenched with H_2O. The mixture was filtered through a *Celite* pad, the whole filtrate was concentrated *in vacuo*, and extracted with AcOEt. The org. extract was washed with brine, dried (Na_2SO_4), and evaporated. The crude mixture was purified by CC (SiO_2; AcOEt/hexane 25:75) to provide **4** (4.69 g, 93%). Colorless liquid. IR (neat): 3448, 2951, 1732, 1517, 1271, 1236, 1205, 1155, 1034, 819. ^1H-NMR (300 MHz, $CDCl_3$): 6.77 (*d*, *J* = 8.3, 1 H); 6.67–6.62 (*m*, 2 H); 4.10 (*q*, *J* = 7.5, 2 H); 3.88 (*s*, 3 H), 2.85 (*t*, *J* = 7.5, 2 H); 2.54 (*t*, *J* = 7.5, 2 H); 1.24 (*t*, *J* = 7.5, 3 H). ^{13}C-NMR (75 MHz,

$CDCl_3$): 172.9; 146.3; 143.8; 132.3; 120.6; 114.2; 110.8; 60.3; 55.6; 36.2; 30.5; 14.0. ESI-MS: 247 (100, $[M+Na]^+$).

Ethyl 3-(3-Methoxy-4-{[(4-methylphenyl)sulfonyl]oxy}phenyl)propanoate (**5**). To a stirred soln. of **4** (4.5 g, 20.08 mmol) in CH_2Cl_2 (50 ml) was added Et_3N (2.2 g, 20.08 mmol) at 0°, followed by the addition of TsCl (3.83 g, 20.08 mmol). Then, the mixture was stirred at r.t. for 2 h, then diluted with 1N HCl (20 ml) and the layers were separated. The org. layer was washed with sat. aq. $NaHCO_3$ (20 ml) and brine (20 ml). The combined org. layers were dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was purified by CC (SiO_2; AcOEt/hexane 1:9) to give **5** (6.91 g, 91%). Colorless viscous liquid. IR (neat): 2980, 1731, 1599, 1506, 1371, 1178, 1152, 849, 817. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.73 (*d*, *J* = 8.3, 2 H); 7.27 (*d*, *J* = 8.3, 2 H); 7.0 (*d*, *J* = 8.1, 1 H); 6.72–6.63 (*m*, 2 H); 4.1 (*q*, *J* = 7.1, 2 H); 3.56 (*s*, 3 H); 2.88 (*t*, *J* = 7.5, 2 H); 2.56 (*t*, *J* = 7.5, 2 H); 2.45 (*s*, 3 H); 1.23 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 172.5; 151.5; 144.8; 140.8; 136.7; 133.2; 129.2; 128.4; 123.7; 120.1; 112.7; 60.4; 55.4; 35.6; 30.7; 21.5; 14.1. ESI-MS: 396 (100, $[M+NH_4]^+$).

4-[(3S)-3-Hydroxyhex-5-en-1-yl]-2-methoxyphenyl 4-Methylbenzenesulfonate (**6**). To a cooled (−78°) stirred soln. of **5** (2.5 g, 6.61 mmol) in dry CH_2Cl_2 (50 ml) was added DIBAL-H (1.0M; 6.61 ml, 6.61 mmol), and the mixture was stirred for 0.5 h. After completion, the reaction was quenched with sat. sodium potassium tartarate (25 ml) the mixture was stirred for 0.5 h, and then extracted with CH_2Cl_2 (3 × 55 ml). The combined org. phase was washed with brine, dried (Na_2SO_4), and concentrated *in vacuo* to yield a crude product (2.03 g, 92%), which was directly used for the next step.

To the stirred soln. of oven-dried 4-Å molecular sieves (3 g) in CH_2Cl_2 (30 ml) under N_2 were added (*R*)-BINOL (0.214 g, 0.75 mmol) and $Ti(O^iPr)_4$ (0.23 ml, 0.75 mmol). The mixture was heated at reflux for 3 h, and then allowed to cool to r.t., then the crude aldehyde (1.25 g, 3.74 mmol) in CH_2Cl_2 (10 ml), was added. After stirring for 0.5 h at r.t. and cooling to −78°, allyl(tributyl)tin (1.5 ml, 4.86 mmol) was added slowly. The mixture was stirred for an additional 10 min at −78°, then the temp. was raised to −20°, and stirring continued for 24 h. The reaction was quenched with sat. aq. $NaHCO_3$ soln. (50 ml), and the mixture was filtered through a *Celite* pad, and then the two layers were separated. The aq. layer was extracted with CH_2Cl_2 (2 × 20 ml). The combined org. layers were washed with brine (20 ml), dried (Na_2SO_4), and concentrated under reduced pressure to give the crude product, which was purified by CC (AcOEt/hexane 2:8) to give **6** (1.25 g, 89%; 96% ee, determined by chiral HPLC (*CHIRAL PAK IA* column, 250 × 4.6 mm, 5 μm); mobile phase, 20% IPA in hexane; flow rate, 1.0 ml/min; detection, 210 nm; t_R 12.406 min). Viscous liquid: $[\alpha]_D^{25} = -4.0$ (*c* = 0.2, $CHCl_3$). IR (neat): 3422, 2926, 1599, 1505, 1369, 1176, 1090, 851. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.75 (*d*, *J* = 8.3, 2 H); 7.29 (*d*, *J* = 7.9, 2 H); 7.01 (*d*, *J* = 8.1, 1 H); 6.73–6.64 (*m*, 2 H); 5.88–5.72 (*m*, 1 H); 5.15 (*dd*, *J* = 10.9, 5.3, 2 H); 3.69–3.58 (*m*, 1 H); 3.56 (*s*, 3 H); 2.83–2.70 (*m*, 1 H); 2.69–2.56 (*m*, 1 H); 2.45 (*s*, 3 H); 2.37–2.25 (*m*, 1 H); 2.22–2.09 (*m*, 1 H); 1.79–1.68 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 151.4; 144.8; 142.4; 136.4; 134.4; 133.3; 129.2; 128.5; 123.6; 120.2; 118.4; 112.8; 69.7; 55.4; 42.0; 38.1; 31.9; 21.6. ESI-MS: 399 (100, $[M+Na]^+$).

4-[(3S,5E)-3-Hydroxy-7-(4-hydroxyphenyl)hept-5-en-1-yl]-2-methoxyphenyl 4-Methylbenzenesulfonate (**7**). To a soln. of **6** (150 mg, 0.39 mmol) in CH_2Cl_2 (150 ml) were added *Grubbs*' second generation catalyst (17 mg, 0.02 mmol) and *chavicol* (**9**; 267 mg, 1.99 mmol) at r.t., and the mixture was stirred at 40° for 2 h. The mixture was concentrated *in vacuo* to give a crude product which was purified by CC (AcOEt/hexane 4:6) to give **7** (155 mg, 81%). Colorless viscous liquid. $[\alpha]_D^{25} = -9.0$ (*c* = 0.2, $CHCl_3$). IR (neat): 3452, 2926, 1599, 1509, 1366, 1175, 1090, 851, 817. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.74 (*d*, *J* = 8.3, 2 H); 7.27 (*d*, *J* = 9.4, 2 H); 7.00–6.88 (*m*, 3 H); 6.68–6.58 (*m*, 4 H); 5.64 (*dt*, *J* = 15.1, 6.6, 1 H); 5.42 (*dt*, *J* = 15.1, 7.1, 1 H); 3.68–3.57 (*m*, 1 H); 3.52 (*s*, 3 H); 3.24 (*d*, *J* = 6.6, 2 H); 2.80–2.66 (*m*, 1 H); 2.64–2.51 (*m*, 1 H); 2.44 (*s*, 3 H); 2.35–2.09 (*m*, 2 H); 1.79–1.63 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.1; 151.4; 144.9; 142.4; 136.3; 133.8; 133.1; 132.0; 129.4; 129.3; 128.5; 126.4; 123.6; 120.2; 115.2; 112.8; 70.3; 55.4; 40.6; 38.1; 38.0; 31.8; 21.6. ESI-MS: 505 (100, $[M+Na]^+$).

4-[(3S,5E)-3-Hydroxy-7-(4-hydroxyphenyl)hept-5-en-1-yl]-2-methoxyphenol (**8**). To a soln. of **7** (90 mg, 0.18 mmol) in MeOH (10 ml) was added K_2CO_3 (150 mg, 1.08 mmol), and the mixture was heated at reflux temp. for 2 h, cooled to 0°, and acidified with 1M HCl to pH 2. The combined soln. was extracted with AcOEt (3 × 20 ml), washed with brine (15 ml), dried (Na_2SO_4), and concentrated *in vacuo*. Purification by CC (AcOEt/hexane 6:4) afforded **8** (49 mg, 80%). Colorless viscous liquid. $[\alpha]_D^{25} = -16.50$ (*c* = 0.2, $CHCl_3$). IR (neat): 3413, 2926, 1513, 1266, 1232, 1152, 1032, 770. ^{1}H-NMR

(300 MHz, $CDCl_3$): 7.02 (*d*, *J* = 8.3, 2 H); 6.83 (*d*, *J* = 7.5, 1 H); 6.78–6.64 (*m*, 4 H); 5.69 (*dt*, *J* = 15.1, 6.7, 1 H); 5.48 (*dt*, *J* = 15.1, 7.5, 1 H); 3.86 (*s*, 3 H); 3.71–3.60 (*m*, 1 H); 3.29 (*d*, *J* = 6.8, 2 H); 2.79–2.54 (*m*, 2 H); 2.28–2.23 (*m*, 1 H); 2.21–2.09 (*m*, 1 H); 1.81–1.70 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.0; 146.3; 143.5; 133.9; 133.6; 132.1; 129.4; 126.6; 120.8; 115.2; 114.2; 111.0; 70.3; 55.8; 40.5; 38.5; 38.1; 31.5. ESI-MS: 351 (100, $[M + Na]^+$).

Rhoiptelol C (= *(2*S*,3*S*,5*S*)-7-(4-Hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)heptane-2,3,5-triol*; **1**) [3]. *AD-mix-α* (42.6 mg, 1.4 g/mmol) and methanesulfonamide (39 mg, 4.2 mmol) was added to ^{t}BuOH/H_2O (1:1; 10 ml), the mixture was stirred at r.t. for 10 min and then cooled to 0°. To this soln. was added **8** (10 mg, 0.03 mmol), and the mixture was stirred for 24 h at 0°. The reaction was quenched with solid Na_2SO_3 (100 mg) at r.t., and the mixture was diluted with AcOEt (50 ml). The aq. layer was extracted with AcOEt (3 × 20 ml), and the combined org. layer washed with brine (10 ml) and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified by CC (AcOEt/hexane 8:2) to afford **1** (8 mg, 75%). White solid. $[\alpha]_D^{25} = -21$ (*c* = 0.4, MeOH). IR (KBr): 3423, 2922, 2853, 1515, 1458, 1263, 1032, 770. ^{1}H-NMR (300 MHz, (D_6)acetone/D_2O): 7.07 (*d*, *J* = 8.1, 2 H); 6.80 (*d*, *J* = 1.9, 1 H); 6.73 (*d*, *J* = 8.1, 2 H); 6.71 (*d*, *J* = 8.1, 2 H); 6.63 (*dd*, *J* = 8.1, 1.9, 1 H); 3.81 (*m*, 1 H); 3.80 (*s*, 3 H); 3.73–3.52 (*m*, 2 H); 2.79 (*dd*, *J* = 13.7, 4.9, 1 H); 2.71–2.50 (*m*, 2 H); 1.76–1.60 (*m*, 4 H). ^{13}C-NMR (75 MHz, (D_6)acetone/D_2O): 156.4; 148.1; 145.3; 134.7; 131.2; 131.1; 121.4; 115.7; 115.5; 112.7; 76.2; 73.8; 71.1; 56.1; 41.0; 40.5; 39.4; 32.0. HR-ESI-MS: 385.1622 ($C_{20}H_{26}NaO_6^+$, $[M + Na]^+$; calc. 385.1627).

REFERENCES

[1] P. Claeson, P. Tuchinda, V. Reutrakul, *J. Indian Chem. Soc.* **1994**, *71*, 509; G. M. Keserü, M. Nógrádi, *Stud. Nat. Prod. Chem.* **1995**, *17*, 357; P. Claeson, U. P. Claeson, P. Tuchinda, V. Reutrakul, *Stud. Nat. Prod. Chem.* **2002**, *26*, 881; H. Lv, G. She, *Nat. Prod. Commun.* **2010**, *5*, 1687.

[2] G. J. Fan, Y. H. Kang, Y. N. Han, B. H. Han, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6720; N. X. Nhiem, P. V. Kiem, C. V. Minh, N. Kim, S. Park, H. Y. Lee, E. S. Kim, Y. H. Kim, S. Kim, Y.-S. Koh, S. H. Kim, *J. Nat. Prod.* **2013**, *76*, 495; H. Mohamad, N. H. Lajis, F. Abas, A. M. Ali, M. A. Sukari, H. Kikuzaki, N. Nakatani, *J. Nat. Prod.* **2005**, *68*, 285; M. S. Ali, Y. Tezuka, S. Awale, A. H. Banskota, S. Kadota, *J. Nat. Prod.* **2001**, *64*, 289; D. Shin, K. Kinoshita, K. Koyama, K. Takahashi, *J. Nat. Prod.* **2002**, *65*, 1315; H. Wohlmuth, M. A. Deseo, D. J. Brushett, D. R. Thompson, G. MacFarlane, L. M. Stevenson, D. N. Leach, *J. Nat. Prod.* **2010**, *73*, 743.

[3] Z.-H. Jiang, T. Tanaka, H. Hirata, R. Fukuoka, I. Kouno, *Phytochemistry* **1996**, *43*, 1049; H.-C. Wu, M.-J. Cheng, C.-F. Peng, S.-C. Yang, H.-S. Chang, C.-H. Lin, C.-J. Wang, I.-S. Chen, *Phytochemistry* **2012**, *82*, 118.

[4] S. P. Reddy, K. Ashalatha, D. K. Reddy, B. Chinnababu, Y. Venkateswarlu, *Synthesis* **2011**, *19*, 3180; S. P. Reddy, B. Chinnababu, V. Shekhar, D. K. Reddy, G. V. S. Bhanuprakash, L. R. Velatoor, J. V. Rao, Y. Venkateswarlu, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 4182; M. Narasimhulu, T. S. Reddy, K. C. Mahesh, A. S. Krishna, J. V. Rao, Y. Venkateswarlu, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3125.

[5] a) L. X. Yang, K. X. Huang, H. B. Li, J. X. Gong, F. Wang, Y. B. Feng, Q. F. Tao, Y. H. Wu, X. K. Li, X. M. Wu, S. Zeng, S. Spencer, Y. Zhao, J. Qu, *J. Med. Chem.* **2009**, *52*, 7732; b) U. Ramulu, D. Ramesh, S. Rajaram, S. P. Reddy, K. Venkatesham, Y. Venkateswarlu, *Tetrahedron: Assymetry* **2012**, *23*, 117.

[6] J. J. Beck, J. H. Kim, B. C. Campbell, S.-C. Chou, *J. Nat. Prod.* **2007**, *70*, 779.

[7] G. E. Keck, K. H. Tarbet, L. S. Geraci, *J. Am. Chem. Soc.* **1993**, *115*, 8467; B. Chinnababu, S. P. Reddy, C. B. Rao, K. Rajesh, Y. Venkateswarlu, *Helv. Chim. Acta* **2010**, *93*, 1960.

[8] A. K. Chatterjee, T.-L. Choi, D. P. Sanders, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 11360; H. E. Blackwell, D. J. O'Leary, A. K. Chatterjee, R. A. Washenfelder, D. A. Bussmann, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 58.

[9] H. C. Kolb, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483.

Received November 5, 2013