Syntheses of (±)-Curcuphenol, (±)-Curcudiol and (±)-Curcuhydroquinone: A Johnson-Claisen Rearrangement Approach

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The synthesis of (±)-curcuphenol **1**, (±)-curcudiol **2**, (±)-curcuhydroquinone **3** and (±)-curcuquinone **4** had been achieved, in which the Johnson-Claisen rearrangement was used as key step.

Keywords: (±)-Curcuphenol; (±)-Curcudiol; (±)-Curcuhydroquinone; (±)-Curcuquinone; Synthesis.

INTRODUCTION

Sesquiterpenes are a big family naturally occurring compounds which could be found in many kinds of plants or microorganisms.[1,4] The aromatic bisabolane sesquiterpenes are a small branch of them which have the simplest monocarbocyclic skeleton and have been popular synthetic targets globally in last 30 years.[2] Their parent hydrocarbons skeleton is shown in Figure 1, and many of them had been recognized as odor component of many plant essential oils.[3] (+)-Curcuphenol and (+)-curcudiol were firstly isolated from the water collection of the sponge *Didiscus flavus*. (+)-Curcuphenol was found to be an inhibitor of gastric H, K-ATPase and to have antitumor and antifungal activities.[4] (-)-Curcuphenol, (-)-curcuhydroquinone and (-)-curcuquinone were isolated from the Caribbean gorgonian *Pseudopterogorgia rigida* and showed antibacterial activity against *Staphylococcus aureus* and the marine pathogen *Vibro anguillarum*.[5] Curcuhydroquinone and curcuquinone have been used for synthesis of some helianuols,[6] one kind of allelochemicals isolated from sunflower *Helianthus annuus* leaves bearing significant biological activity. Because of their wide range of biological activities, these compounds and their derivatives are attractive synthetic targets, and especially to verify the usefulness of newly developed synthetic methodology. Although several report of the synthesis this kind of compounds can be found in literature, the existent routes are either long or inefficient.[7]

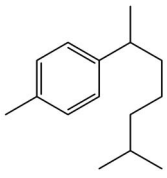


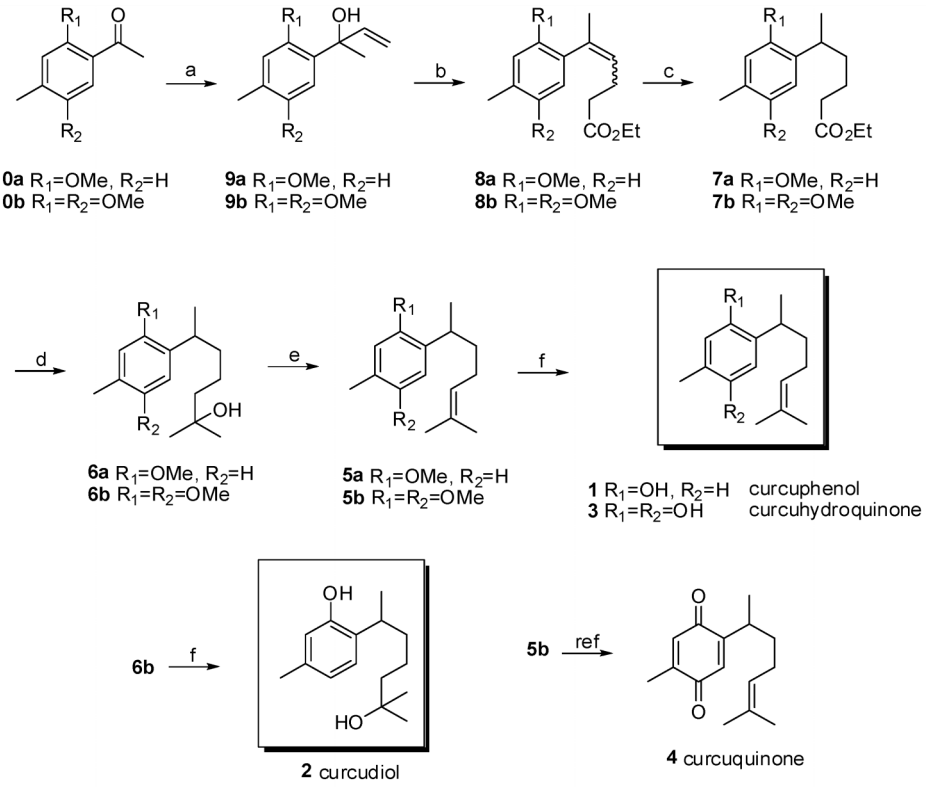
Fig. 1. Aromatic bisabolane sesquiterpenes skeleton.

Johnson-Claisen rearrangement is a powerful tool in synthesis of naturally occurring products in which a key intermediate of derivatives of -unsaturated pentanoic acid was involved.[8] As an extension of our continuous effort to synthesize those kinds of naturally occurring products and to evaluate their potential in agrochemicals,[9] herein, we wish to report the synthesis of (±)-curcuphenol **1**, (±)-curcudiol **2**, (±)-curcuhydroquinone **3** and (±)-curcuquinone **4** through a Johnson-Claisen rearrangement approach.

RESULTS AND DISSCUSION

As shown in Scheme I, our synthesis commenced at acetophenones **10a** and **10b**, carbinols **9a** and **9b** will be given after a Grignard addition in 90 and 93% yield, respectively. If anhydrous $CeCl_3$ was not used, the yield is low, relatively. The carbinols underwent a Johnson-Claisen rearrangement in $CH_3C(OEt)_3$ and at the catalysis of propanoic acid at 170 °C for 3 days, to give compound **8a** and **8b** in good yield as an *E/Z* mixtures in which the ratio of *E* and *Z* isomer is in *ca.* 3:1. If the rearrangement was performed in a microwave oven with irradiation, the reaction duration can be reduced to 15-30 minutes without loss of yields. With this key intermediate in hand, the double bonds were reduced after catalytic hydrogen to furnish **7a** and **7b** in excellent yields. Compounds **7a** and **7b** were subjected to an excess MeMgI addition to afford the tertiary alcohol **6a** and **6b**. (±)-Curcudiol **2** was obtained after a

Scheme I



Reagents and conditions:

a) CH_2=CHMgBr, $CeCl_3$, 0 °C-r.t.; b) $CH_3C(OEt)_3$, EtCOOH, 170 °C, 3d, or MWI;
c) H_2, 5% Pd/C, EtOAc; d) 4 eq MeMgI, THF, 0 °C-r.t.; e) I_2, THF, reflux;
f) EtSNa, DMF, 130 °C or pure MeMgI.

demethylation step of compound **6b** using NaSEt in 96% yield. The dehydrated products **5b** and **5b** were got in very high yield at dehydration protocol at presence I_2, respectively. Compounds **5a** and **5b** can be converted to (±)-curcuphenol **1**, (±)-curcuhydroquinone **3** and using a NaSEt demethylation protocol in 95 and 90% yields, respectively. (±)-Cucuquinone **4** can be obtained through oxidation of **5b** on the basis of the reference reported by Ono and coworkers.[7a] The spectrums of target molecules are identical to the ones in literature. It is obvious that our synthetic route is terse and effective.

CONCLUSION

In summary, we have achieved an effective and facile route to synthesis of (±)-curcuphenol **1**, (±)-curcudiol **2**, (±)-curcuhydroquinone **3** and (±)-curcuquinone **4** in higher yield using cheap starting materials. The Johnson-Claisen rearrangement was used to build up the key intermediate is our salient characteristic of our approach.

EXPERIMENTAL

General

The IR spectra were recorded on a Perkin-Elmer 2000 FTIR spectrometer. ^{1}H and ^{13}C NMR data were recorded in $CDCl_3$ with Bruker-400 or Virian 300 spectrometers if not noted otherwise. The chemical shifts were reported in ppm relative to TMS. Mass spectra were recorded on a HP-5988 mass spectrometer (EI). HRMS (ESI) were performed on a Bruker FT-MS analyzer. Column chromatography were generally performed on silica gel (200-300 mesh) eluting with petroleum ether:EtOAc (100:1-10:1 v/v) and TLC inspections on silica gel GF254 plates with petroleum ether: EtOAc (20:1-5:1 v/v) if not noted otherwise.

2-(2-Methoxy-4-methylphenyl)but-3-en-2-ol **9a**: To a solution of 2-methoxy-4-methylphenoacetone (6.4 g, 0.04 mol) in anhydrous THF (60 mL) was added anhydrous $CeCl_3$ (3.94 g, 0.016 mol) and then added magnesium vinyl bromide (80 mL, 1 mol/L in THF) dropwise at -30 °C, and the resulting mixture was stirred for 2 hours and warmed to

room temperature. The saturated NH_4Cl was introduced to quench the reaction. The reaction mixture was extracted with ethyl acetate (3 × 100 mL); the combined organic layers were washed with brine and dried with anhydrous Na_2SO_4. The solvent was evaporated in vacuum and the residue was purified through column chromatography to give **9a** (6.9 g, 90%) as a pale yellow oil. ^{1}H-NMR: 1.66 (s, 3H), 2.35 (s, 3H), 3.87 (s, 3H), 4.42 (s, 1H), 5.04, (dd, 1H, *J* = 10.8 Hz, *J* = 1.2 Hz), 5.14 (dd, 1H, *J* = 17.2 Hz, *J* = 1.2 Hz), 6.18 (dd, 1H, *J* = 17.6 Hz, *J* = 10.8 Hz), 6.751 (s, 1H), 6.77 (d, 1H, *J* = 8 Hz), 7.20 (d, 1H, *J* = 8 Hz). ^{13}C-NMR: 22.3, 27.2, 55.4, 74.7, 111.3, 112.5, 121.4, 126.4, 130.8, 138.5, 145.0, 156.9. ESI-MS: M+Na = 175.2.

2-(2,5-Dimethoxy-4-methylphenyl)but-3-en-2-ol **9b**: **9b** was obtained from **10b** by method similar to **9a** as a yellowish oil in 93% yield. ^{1}H-NMR: 1.68 (s, 3H), 2.22 (s, 3H), 3.80 (s, 3H), 3.83 (s, 3H), 4.44 (s, 1H), 5.07 (dd, 1H, *J* = 10.8 Hz, *J* = 1.2 Hz), 5.16 (dd, 1H, *J* = 17.2 Hz, *J* = 1.2 Hz), 6.18 (dd, 1H, *J* = 17.2 Hz, *J* = 10.8 Hz), 6.75 (s, 1H), 6.84 (s, 1H). ^{13}C-NMR: 16.0, 27.3, 56.0, 56.1, 74.7, 109.5, 111.5, 114.9, 126.2, 131.8, 144.9, 150.5, 151.6. ESI-MS: M+H-H_2O = 205.3.

Ethyl 5-(2-methoxy-4-methylphenyl)hexenoate **8a**: A mixture of **9a** (7.69 g, 0.04 mol), triethyl orthoacetate (32.7 g, 0.2 mol), propanoic acid (0.15 g, 2 mmol) was warmed to 170 °C for 3 days. The reaction mixture was separated through column chromatography directly to afford crude **8a** (mixtures of *E* and *Z*) as pale yellow oil (80%). ESI-MS: M+H = 263.3.

Ehyl 5-(2,5-dimethoxy-4-methylphenyl)hexenoate **8b**: **8b** was obtained from **9b** similarly in 84% yield. ESI-MS: M+Na = 315.3.

Ethyl 5-(4-methyl-2-methoxylphenyl)hexanoate **7a**: To the solution of **8a** (2.62 g, 10 mmol) in a mixture of ethyl acetate (70 mL) and acetic acid (10 mL) was added 10% Pd/C (200 mg). The atmosphere was excavated by H_2 three times, and the reaction mixture was stirred for 24 h at the atmosphere of 1.5 atm H_2. The Pd/C was filtered and the filtrate was evaporated in vacuum and the residue was purified through column chromatography to give **7a** (2.45 g, 98%) as a pale yellow oil. ^{1}H-NMR: 1.19 (d, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.53-1.61 (m, 4H), 2.26-2.29 (m, 2H), 2.33 (s, 3H), 3.14-3.18 (m, 1H), 3.80 (s, 1H), 4.11 (q, 2H, *J* = 7.2 Hz), 6.68 (s, 1H), 6.75 (d, 1H, *J* = 7.6 Hz), 7.03 (d, 1H, *J* = 7.6 Hz). ^{13}C-NMR: 14.2, 21.0, 21.4, 23.1, 31.1, 34.4, 36.6, 55.3, 60.0, 111.4, 121.1, 126.4, 132.3, 136.4, 156.8, 174.8. ESI-MS: M^+ = 264.

Ethyl 5-(4-methyl-2,5-dimethoxylphenyl)hexanoate **7b** was obtained from **8b** by above method similarly as a pale yellow oil in 95% yield. ^{1}H-NMR: 1.17 (d, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 2.20 (s, 3H), 2.27-2.29 (m, 2H), 3.16-3.25 (m, 1H), 3.77 (s, 3H), 3.80 (s, 3H), 4.11 (q, 2H, *J* = 7.2 Hz), 6.67 (s, 1H), 6.70 (s, 1H). ^{13}C-NMR: 14.2, 16.1, 21.1, 23.1, 31.6, 34.3, 36.7, 56.1, 56.3, 60.1, 109.6, 114.2, 124.3, 133.4, 150.7, 151.8, 173.8. ESI-MS: M^+ = 294.

2-Methyl-6-(4-methyl-2-methoxylphenyl)-2-heptanol **6a**: To a suspension of power Mg (1.45 g, 60 mmol) in 50 mL of anhydrous diethyl ether was added slowly iodomethane (6.39 g, 45 mmol) in 50 mL of anhydrous diethyl ether at reflux. After completion, the reaction mixture was stirred at reflux for 1 h and was cooled to room temperature. A solution of compound **7a** (2.25 g, 9 mmol) in anhydrous diethyl ether (30 mL) was added slowly to the above reaction mixture at room temperature. The reaction was refluxed for 1 h and quenched with saturated NH_4Cl and extracted with ethyl acetate (3 × 70 mL). The combined organic layer was washed with saturated $NaHCO_3$ and brine, dried with anhydrous $MgSO_4$. The solvent was evaporated in vacuum and the residue was purified through column chromatography to give **6a** (2.10 g, 93%) as colorless oil. ^{1}H-NMR: 1.14 (s, 3H), 1.18 (s, 3H), 1.21 (d, *J* = 7.2 Hz, 3H), 1.30-1.65 (m, 6H), 2.33 (s, 3H), 3.18-3.25 (m, 1H), 3.84 (s, 3H), 6.71 (s, 1H), 6.78 (d, 1H, *J* = 7.8 Hz), 7.01 (d, 1H, *J* = 7.8 Hz). ^{13}C-NMR: 21.0, 21.2, 22.3, 29.0, 29.1, 31.2, 37.6, 43.8, 55.2, 70.8, 111.4, 121.1, 126.4, 132.8, 136.1, 156.7. EIMS (*m/z*): 250, 235, 232, 217, 175, 162, 149, 119, 91.

2-Methyl-6-(4-methyl-2,5-dimethoxylphenyl)-2-heptanol **6b** was obtained from **7b** by method similar to **6a** (89%) as colorless oil. ^{1}H-NMR: 1.18 (s, 3H), 1.20 (s, 3H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.30-1.65 (m, 6H), 2.34 (s, 3H), 3.18-3.26 (m, 1H), 3.83 (s, 3H), 3.87 (s, 3H), 6.65 (s, 1H), 6.74 (s, 1H). ^{13}C-NMR: 16.0, 17.9, 21.1, 22.3, 29.0, 31.7, 37.4, 43.9, 56.1, 56.3, 70.9, 109.7, 114.3, 124.2, 134.0, 150.7, 151.8. EIMS (*m/z*): 280, 265, 262, 247, 205, 192, 179, 149, 119, 91.

2-Methyl-6-(4-methyl-2-methoxylphenyl)-2-heptene **5a**: To a solution of compound **6a** (2.00 g, 8 mmol) in benzene (100 mL) was added *p*-TosOH acid (100 mg) and equipped a Dead-Stark trap. The reaction mixture was refluxed for 6 h and then diluted with ethyl acetate (100 mL). The organic layer was washed with saturated $NaHCO_3$ and brine, dried with anhydrous $MgSO_4$. The solvent was evap-

orated in vacuum and the residue was purified through column chromatography to give **5a** (1.76 g, 95%) as a colorless oil. ^{1}H-NMR: 1.19 (d, J = 7.0 Hz, 3H), 1.48-1.65 (m, 2H), 1.55 (s, 3H), 1.69 (s, 3H), 1.88-2.07 (m, 2H), 2.35 (s, 3H), 3.15 (sex, J = 7.0 Hz, 1H), 3.82 (s, 3H), 5.13 (t, J = 7.0 Hz, 1H), 6.69 (s, 1H), 6.75 (d, J = 7.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H). ^{13}C-NMR: 17.6, 21.1, 21.4, 25.7, 26.3, 31.4, 37.2, 55.3, 111.5, 112.1, 124.9, 126.6, 128.7, 132.9, 136.2, 156.9. EIMS (*m/z*): 232, 217, 189, 175, 162, 149, 119, 91. HRMS: required $C_{16}H_{24}O$ 232.2996, found 232.2990.

2-Methyl-6-(4-methyl-2,5-dimethoxylphenyl)-2-heptene **5b** was obtained from **6b** by method similar to **5a** (96%) as a colorless oil. ^{1}H-NMR: 1.28 (d, J = 7.2 Hz, 3H), 1.56 (s, 3H), 1.57-1.59 (m, 2H), 1.75 (s, 3H), 1.96-2.04 (m, 2H), 2.33 (s, 3H), 3.21-3.26 (m, 1H), 3.87 (s, 3H), 3.88 (s, 3H), 5.22 (t, J = 6.9 Hz, 1H), 6.67 (s, 1H), 6.70 (s, 1H). ^{13}C-NMR: 16.0, 17.5, 21.2, 25.6, 26.3, 31.8, 37.3, 56.0, 56.3, 111.6, 112.5, 122.0, 125.0, 126.7, 133.1, 136.8, 157.1. EIMS (*m/z*): 262, 247, 219, 192, 179, 149, 119, 91. HRMS: required $C_{17}H_{27}O_2$ 262.2013, found 262.2009.

(±)-Curcuphenol **1**: To DMF (3 mL) was added ethanethiol (147 mg, 2.36 mmol) and NaH in 60% mineral oil (94 mg, 2.36 mmol), after hydrogen evolved ceased (about 30 minutes) and then compound **5a** (110 mg, 0.47 mmol) in DMF (1 mL) was added. The mixture was heated to 130 °C and stirred for 4 h. The reaction was cooled to room temperature, quenched by saturated ammonium chloride and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation, the residue was purified through column chromatography to give **1** (98 mg, 95%) as a colorless oil. IR (neat): 3537, 2965, 2935, 2866, 1664, 1617, 1421, 808 cm^{-1}. ^{1}H-NMR: 1.22 (d, J = 7.0 Hz, 3H), 1.54 (s, 3H), 1.55-1.69 (m, 2H), 1.68 (s, 3H), 1.89-1.97 (m, 2H), 2.27 (s, 3H), 2.96 (sextet, J = 7.0 Hz, 1H), 4.67 (s, 1H), 5.13 (br, 1H), 6.59 (br, 1H), 6.72 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H). ^{13}C-NMR: 17.7, 20.8, 21.1, 25.7, 26.1, 31.4, 37.3, 116.2, 121.7, 124.6, 126.8, 130.0, 132.0, 136.5, 152.8. MS (EI): 218, 203, 161, 148, 138, 119, 91, 77. HRMS: required $C_{15}H_{22}O$, 218.1751, found 218.1743.

(±)-Curcudiol **2**: To DMF (3 mL) was added ethanethiol (150 mg, 2.37 mmol) and NaH in 60% mineral oil (95 mg, 2.37 mmol), after hydrogen evolved ceased (about 30 minutes) and then compound **6a** (89 mg, 0.36 mmol) in DMF (1 mL) was added. The mixture was heated to 130 °C and stirred for 4 h. The reaction was cooled to room temperature, quenched by saturated ammonium chloride and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation, the residue was purified through column chromatography to give **2** (82 mg, 96%) as a colorless oil. IR (neat): 1070, 1420, 1254, 1619, 1711, 2859, 2924 cm^{-1}. ^{1}H-NMR: 1.18 (s, 3H), 1.20 (s, 3H), 1.30 (d, J = 7.8 Hz, 3H), 1.33-1.72 (m, 6H), 2.05 (br, 1H), 2.23 (s, 3H), 3.15-3.18 (m, 1H), 5.02 (br, 1H), 6.61 (s, 1H), 6.78 (d, J = 7.8 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H). ^{13}C-NMR: 21.16, 22.23, 28.99, 29.61, 31.47, 37.96, 43.75, 71.93, 116.60, 121.40, 126.97, 131.07, 136.40, 153.70. MS (EI): 236, 218, 203, 161, 148, 135, 121, 91. HRMS: required $C_{15}H_{24}O_2$, 236.1856, found 236.1853.

(±)-Curcuhydroquinone **3**: To a suspension Mg (1.45 g, 60 mmol) in 10 mL of anhydrous diethyl ether was added slowly iodomethane (6.35 g, 45 mmol) in anhydrous diethyl ether at room temperature. After completion, the reaction mixture was refluxed for 1 h and then the mixture was evaporated in vacuum. The neat compound **5b** (393 mg, 1.5 mmol) was added to the above residue and heated to 180 °C for 15 minutes, after cooled to room temperature and 100 mL 1.0 M HCl was added to quench the reaction. The mixture was extracted EtOAc (3 × 20 mL); the combined organic layer was washed with brine and dried over Na_2SO_4. After evaporation the residue was purified through column chromatography to give **3** (316 mg, 90%) as a colorless oil. IR (neat): 3545, 2966, 2927, 1666, 1615, 1456, 1417, 1377, 1306, 1187, 1003, 875, 833 cm^{-1}. ^{1}H-NMR: 1.20 (d, J = 7.2 Hz, 3H), 1.53 (s, 3H), 1.50-1.63 (m, 2H), 1.68 (s, 3H), 1.92-1.95 (m, 2H), 2.17 (s, 3H), 2.94 (m, 1H), 4.65 (br, 1H), 5.15 (br, 1H), 6.56 (br, 1H), 6.71 (br, 1H), 7.02 (d, J = 7.9 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 300 MHz): 15.4, 17.7, 21.1, 25.7, 26.0, 31.5, 37.4, 113.5, 118.0, 121.8, 124.6, 131.8, 132.1, 146.7, 147.8. MS (EI): 235 (M^+ + 1), 234, 217, 191, 177, 164, 151, 137, 124, 107, 95, 77. HRMS: required $C_{15}H_{22}O_2$, 234.1700, found 234.1703.

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REFERENCES

1. (a) Pedersen, M. M.; Chukwujekwu, J. C.; Lategan, C. A.;

Staden, J.; Smith, P. J.; Staerk, D. *Phytochemistry* **2009**, *70*, 601. (b) Takeda, Y.; Masuda, T.; Morikawa, H.; Ayabe, H.; Hirata, E.; Shinzato, T.; Aramoto, M.; Otsuka, H. *Phytochemistry* **2005**, *66*, 727. (c) Chen, C. M.; Lin, F. W.; Kuo, P. C.; Shi, L. S.; Wang, J. J.; Wu, T. S. *J. Chin. Chem. Soc.* **2001**, *48*, 933. (d) Dai, J. Q.; Hou, Z. F.; Zhu, Q. X.; Yang, Li; Li, Y. *J. Chin. Chem. Soc.* **2001**, *48*, 249. (e) Gao, K.; Jia, Z. J. *J. Chin. Chem. Soc.* **2004**, *51*, 417. (f) El-Razek, M. H. A.; Wu, Y. C.; Chang, F. R. *J. Chin. Chem. Soc.* **2007**, *54*, 235.

2. (a) Vyvyan, J. R.; Brown, R. C.; Woods, B. P. *J. Org. Chem.* **2009**, *74*, 1374. (b) Braun, N. A.; Spitzner, D. *Arkivoc* **2007**, 273. (c) Serra, S. *Synlett* **2000**, 890. (d) Vyvyan, J. R.; Loitz, C.; Looper, R. E.; Mattingly, C. S.; Peterson, E. A.; Staben, S. T. *J. Org. Chem.* **2004**, *69*, 2461. (e) Zhang, C. X.; Ito, S.; Hosoda, N.; Asami, M. *Tetrahedron Lett.* **2008**, *49*, 2552. (f) Lu, J. P.; Xie, X. G.; Chen, B.; She, X. G.; Pan, X. F. *Tetrahedron: Asymmetry* **2005**, *16*, 1435. (g) Ono, M.; Ogura, Y.; Hatogai, K.; Akita, H. *Chem. Pharm. Bull.* **2001**, *49*, 1581. (h) Hagiwara, H.; Okabe, T.; Ono, H.; Kamat, V. P.; Hoshi, T.; Suzuki, T.; Ando, M. *J. Chem. Soc., Perkin Trans. 1* **2002**, 895. (i) Kim, S. G.; Kim, J.; Jung, H. *Tetrahedron Lett.* **2005**, *46*, 2437. (j) Fuganti, C.; Serra, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3758. (k) Ono, M.; Ogura, Y.; Hatogai, K.; Akita, H. *Tetrahedron: Asymmetry* **1995**, *6*, 1829.
3. (a) Honwad, V. K.; Rao, A. S. *Tetrahedron* **1965**, *21*, 2593. (b) Damodaran, N. P.; Dev, S. *Tetrahedron* **1965**, *21*, 4113.
4. (a) Fusetani, N.; Sugano, M.; Matsunaga, S.; Hashimoto, K. *Experentia* **1987**, *43*, 1234. (b) Wright, A. E.; Pomponi, S. A.; McConnell, O. J.; Komoto, S.; McCarthy, P. J. *J. Nat. Prod.* **1987**, *50*, 976.
5. McEnroe, F. J. F., W. *Tetrahedron* **1978**, *34*, 1661.
6. (a) Macias, F. A.; Chinchilla, D.; Molinillo, J. M. G.; Marin, D.; Varela, R. M.; Torres, A. *Tetrahedron* **2003**, *59*, 1679. (b) Macias, F. A.; Torres, A.; Galindo, J. L. G.; Varela, R. M.; Alvarez, J. A.; Molinillo, J. M. G. *Phytochemistry* **2002**, *61*, 687.
7. (a) Ono, M.; Yamamoto, Y.; Akita, H. *Chem. Pharm. Bull.* **1995**, *43*, 553. (b) Vickers, T. D.; Keay, B. A. *Synlett* **2003**, 1349.
8. (a) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.-T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741. (b) Birman, V. B.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2002**, *124*, 2080. (c) Schlama, T.; Baati, R.; Gouverneur, V.; Valleix, A.; Falck, J. R.; Mioskowski, C. *Angew. Chem. Int. Ed.* **1998**, *37*, 2085. (d) Ng, F. W.; Lin, H.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2002**, *124*, 9812. (e) Kim, D.; Lee, J.; Shim, P. J.; Lim, J. I.; Jo, H.; Kim, S. *J. Org. Chem.* **2002**, *67*, 764.
9. (a) Du, Z. T.; Li, A. P.; Peng, K.; Wu, T. X.; Pan, X. F. *J. Chin. Chem. Soc.* **2004**, *51*, 571. (b) Du, Z. T.; She, X. G.; Yue, G. R.; Ma, J. Y.; Li, Y.; Pan, X. F. *Chin. Chem. Lett.* **2004**, *15*, 1389. (c) Li, A. P.; Li, Y.; Du, Z. T.; She, X. G.; Pan, X. F. *Chem. J. Chin. Univ.* **2004**, *25*, 862. (d) Du, Z. T.; Yue, G. R.; Li, A. P.; Ma, J. Y.; Wu, T. X.; She, X. G.; Pan, X. F. *J. Chin. Chem. Soc.* **2004**, *51*, 505.