Krempenes A–D: A Series of Unprecedented Pregnane-Type Steroids from the Marine Soft Coral *Cladiella krempfi*

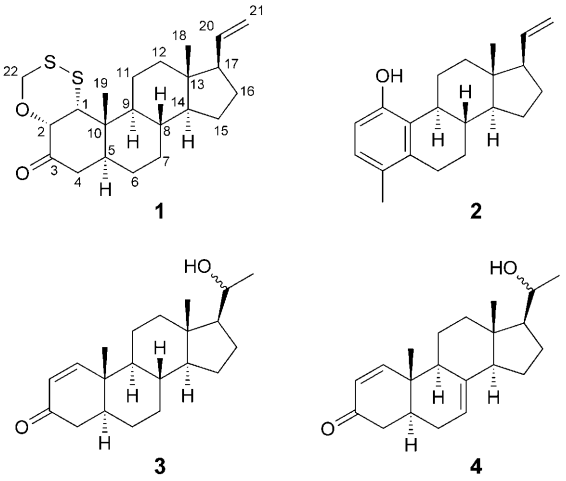
by **Xinping Huang**[a][b][c], **Zhiwei Deng**[d], **Xiaobin Zhu**[a], **Leen van Ofwegen**[e], **Peter Proksch**[f], and **Wenhan Lin***[b]

[a]) Institute of Oceanology, The Chinese Academy of Science, Qingdao 266071, P. R. China
[b]) State Key Laboratory of Natural and Biomimetic Drugs, Peking University, Beijing 100083, P. R. China (phone: +86-10-82806188; fax: +86-10-82802724; e-mail: whlin@hsc.pku.edu.cn)
[c]) Graduate School of the Chinese Academy of Science, Beijing 100039, P. R. China
[d]) Test and Analytic Center, Beijing Normal University, Beijing 100073, P. R. China
[e]) National Museum of Natural History Naturalis, NL-2300 RA Leiden
[f]) Institute of Pharmaceutical Biology and Biotechnology, Heinrich-Heine University, D-40225 Düsseldorf

Four new pregnane-type steroids, krempenes A–D (**1**–**4**), were isolated from the marine soft coral *Cladiella krempfi*. Their structures were elucidated on the basis of 1D- and 2D-NMR analyses, as well as MS experiments. Krempene A (**1**) contains a very unusual structural motif, with a hexacyclic oxadithiino unit fused to the steroidal ring *A*. Krempene B (**2**) is a 19-norpregnane steroid, the 19-Me group formally being transferred to position 4. Furthermore, krempene D contains an unusual C=C bond at C(7) of the pregnane skeleton.

Introduction. – The marine soft corals of the genus *Cladiella* are widely distributed in tropical and subtropical shallow-water habitats. Previous chemical investigations of this genus resulted in various structurally highly diverse metabolites including cembranes [1][2], eunicellane diterpenes [3–11], sesquiterpenes [12], as well as steroids and glycolipides [13–17]. While *C. krempfi* from India was found to mainly contain sclerophytin-type cembranoids and steroids, the same species from the South China Sea is rich of pregnane-type sterols [16–19]. In continuation of our investigations on the chemical diversity from Chinese marine organisms, *C. krempfi* was collected by scuba diving from Hainan Island, South China Sea. As reported previously [19], we isolated two new pregnane glycosides from the corresponding MeOH extract, together with pregna-1,20-dien-3-one and pregna-1,4,20-trien-3-one. In this paper, we report four additional new pregnane derivatives, krempenes A–D (**1**–**4**) from this species.

Results and Discussion. – The molecular formula of compound **1** was determined to be $C_{22}H_{32}O_2S_2$ by HR-FAB-MS (*m*/*z* 393.1916 ($[M+1]^+$; calc. 393.1922)). The IR spectrum displayed absorption bands diagnostic of olefinic (3020) and C=O (1700 cm^{-1}) groups. The ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*, resp.) were characteristic of a pregnane-type sterol related to pregna-20-en-3-one [18]. Detailed 2D-NMR analyses,



including COSY, HMQC, HMBC, and NOESY experiments, led to the identification of **1** as a pregn-20-en-3-one with a fused [1,3,4]oxadithiino ring[1]).

The ^{1}H-NMR spectrum of **1** (*Table 1*) displayed two Me signals at δ(H) 0.64 (*s*) and 1.30 (*s*), and mono-substituted vinyl H-atoms at δ(H) 5.78 (*ddd*, J = 7.4, 11.7, 17.5, H–C(20)), 5.01 (br. *d*, J = 11.7, H_a–C(21)), and 4.98 (br. *d*, J = 17.5 Hz, H_b–C(21)). The ^{13}C-NMR (DEPT) spectrum exhibited 22 carbon resonances: two Me, nine CH_2, eight CH, and three quaternary C-atoms (*Table 2*). The NMR data were characteristic of a pregn-20-ene backbone, closely related to pregna-20-en-3-one [18]. The main difference was in ring *A*, where two CH groups at δ(C) 61.6 (*d*, C(1)) and 76.6 (*d*, C(2)), and a C=O signal at 205.0 (*s*, C(3)) were observed. The COSY correlation between the vicinal H-atoms at δ(H) 4.73 (*d*, J = 4.5, H–C(1)) and 4.35 (*d*, J = 4.5 Hz, H–C(2)), and the HMBC correlations between the H-atom resonance at δ(H) 4.73 and both C(3) and C(19) (δ(C) 15.3 (*q*)) confirmed the position of the C=O group. In addition, the signals at δ(H) 3.80 (*d*, J = 12.4, H_a–C(22)), 4.10 (*d*, J = 12.4 Hz, H_b–C(22)), and δ(C) 51.4 (*t*, C(22)) were assumed to be due to a CH_2 group not being part of ring *A*. The H-atoms of CH_2(22) showed HMBC correlation with the signal at δ(C) 76.6 (*d*, C(2)), which indicated an ether bond between C(2) and C(22). Thus, the remaining degree of unsaturation, required from the molecular formula, in association with two S-atoms, was proposed to be due to a unique [1,3,4]-oxadithiino fused ring between C(1) and C(2).

Regarding the relative configuration of **1**, the tetracyclic steroidal frame was considered to adopt an all-*trans* arrangement typical for pregnane steroids, and supported by NOESY analysis (*Figure*). The NOE correlation between H–C(20) and Me(18) confirmed that the vinyl group at C(17) is β-oriented. The coupling constant J(1,2) of 4.5 Hz implied that H–C(1) and H–C(2) are in axial and equatorial positions, respectively. Further, the correlation from H–C(1) to H–C(2) and Me(19) indicated that both H–C(1) and H–C(2) are in β-orientation.

---

[1]) For systematic names, see the *Exper. Part*.

Table 1. *^{1}H-NMR Data of* **1**–**4**. At 500 MHz in $CDCl_3$; δ in ppm, J in Hz.

Position	**1**	**2**	**3**	**4**
1	4.73 (*d*, *J* = 4.5)	–	7.16 (*d*, *J* = 10.5)	7.04 (*d*, *J* = 10.0)
2	4.35 (*d*, *J* = 4.5)	6.50 (*d*, *J* = 8.0)	5.88 (*d*, *J* = 10.5)	5.93 (*d*, *J* = 10.0)
3		6.87 (*d*, *J* = 8.0)	–	–
4	2.28 (*dd*, *J* = 11.0, 11.0) 2.44 (*dd*, *J* = 2.0, 11.0)	–	2.24 (*dd*, *J* = 4.0, 17.5) 2.37 (*dd*, *J* = 14.0, 17.5)	2.30 (*dd*, *J* = 4.5, 16.5) 2.37 (*dd*, *J* = 13.0, 16.5)
5	2.42 (*ddd*, *J* = 2.0, 11.0, 11.0)	–	1.93–1.95 (*m*)	2.08–2.12 (*m*)
6	1.45–1.48 (*m*) 1.58–1.63 (*m*)	2.67 (*ddd*, *J* = 2.5, 13.0, 13.5) 2.61 (*ddd*, *J* = 5.5, 11.5, 13.5)	1.40–1.42 (*m*) 1.43–1.44 (*m*)	1.80–1.82 (*m*) 2.10–2.13 (*m*)
7	1.01–1.05 (*m*) 1.80–1.82 (*m*)	1.20–1.24 (*m*) 1.82–1.86 (*m*)	0.98–1.01 (*m*) 1.70–1.72 (*m*)	5.31 (br.)
8	1.46–1.49 (*m*)	1.47 (*dddd*, *J* = 1.5, 10.0, 11.0, 11.5)	1.41–1.45 (*m*)	–
9	1.01–1.04 (*m*)	2.45 (*dd*, *J* = 10.0, 10.1)	0.99–1.02 (*m*)	1.96–1.99 (*m*)
11	1.47–1.48 (*m*) 1.82–1.84 (*m*)	1.23 (*dddd*, *J* = 5.0, 10.0, 12.5, 13.5) 2.98 (*dddd*, *J* = 3.0, 3.5, 3.5, 13.5)	1.40–1.44 (*m*) 1.72–1.78 (*m*)	1.55–1.59 (*m*) 1.78–1.80 (*m*)
12	1.20–1.24 (*m*) 1.68–1.70 (*m*)	1.30 (*dd*, *J* = 12.0, 12.5) 1.74 (*ddd*, *J* = 3.0, 3.0, 12.0)	1.19 (*ddd*, *J* = 4.5, 12.5, 12.5) 1.92–1.94 (*m*)	1.28–1.31 (*m*) 1.81–1.84 (*m*)
14	1.03–1.05 (*m*)	1.37 (*ddd*, *J* = 4.5, 11.0, 12.0)	1.14 (*ddd*, *J* = 6.0, 10.0, 10.0)	1.96–1.99 (*m*)
15	1.24–1.28 (*m*) 1.68–1.70 (*m*)	1.34–1.36 (*m*) 1.76–1.79 (*m*)	1.13–1.18 (*m*) 1.56–1.58 (*m*)	1.31–1.32 (*m*) 1.75–1.78 (*m*)
16	1.58–1.60 (*m*) 1.82–1.84 (*m*)	1.59–1.62 (*m*) 1.82–1.86 (*m*)	1.62–1.64 (*m*) 1.91–1.93 (*m*)	1.55–1.58 (*m*) 1.87–1.88 (*m*)
17	2.00 (*ddd*, *J* = 8.0, 9.0, 9.0)	2.10 (*ddd*, *J* = 7.7, 8.5, 8.5)	1.35 (*ddd*, *J* = 8.0, 8.0, 8.0)	1.40–1.42 (*m*)
18	0.64 (*s*)	0.69 (*s*)	0.72 (*s*)	0.60 (*s*)
19	1.30 (*s*)	2.17 (*s*)	1.03 (*s*)	0.98 (*s*)
20	5.78 (*ddd*, *J* = 7.4, 11.7, 17.5)	5.84 (*ddd*, *J* = 7.7, 11.7, 17.5)	3.74 (*dq*, *J* = 6.0, 7.5)	3.75 (*dq*, *J* = 6.0, 7.5)
21	4.98 (*d*, *J* = 17.5) 5.01 (*d*, *J* = 11.7)	5.01 (*d*, *J* = 17.5) 5.03 (*d*, *J* = 11.7)	1.26 (*d*, *J* = 6.0)	1.28 (*d*, *J* = 6.0)
22	4.10 (*d*, *J* = 12.4) 3.80 (*d*, *J* = 12.4)	–	–	–

The molecular formula of **2** was established as $C_{21}H_{28}O$, on the basis of HR-EI-MS (*m*/*z* 296.2132 (M^+; calc. 296.2140) and NMR analysis. The ^{1}H- and ^{13}C-NMR spectra of **2** indicated a pregnane steroid containing an aromatic ring, related to 19-norpregn-1,3,5(10),20-tetraen-3-ol [20]. The 2D-NMR spectroscopic data confirmed the presence of an OH and a Me group at C(1) and C(4) of the aromatic ring *A*, respectively. Thus, the structure of **2** was identified as 4-methyl-19-norpregna-1,3,5(10),20-tetraen-1-ol.

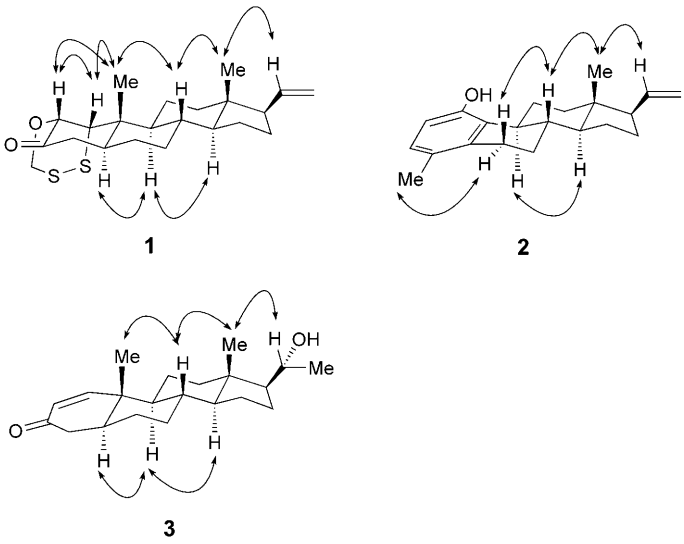


Figure. *Key NOE correlations for* **1**–**3**

The ^{1}H-NMR spectrum of **2** displayed a Me signal at δ(H) 0.69 (*s*) and a monosubstituted vinyl group at 5.84 (*ddd*, $J=7.7, 11.7, 17.5$, H–C(20)), 5.03 (br. *d*, $J=11.7$, H_a–C(21)), and 5.01 (br. *d*, $J=17.5$ Hz, H_b–C(21)). In the ^{13}C-NMR (DEPT) spectrum, 21 C-atoms were observed: two Me, seven CH_2, seven CH, and five quaternary C-atoms. These data are characteristic of a pregnane-type steroid. The presence of six aromatic C-atoms [δ(C) 152.9 (*s*), 112.8 (*d*), 127.4 (*d*), 128.7 (*s*), 138.7 (*s*), and 127.0 (*s*)] were attributed to ring *A*, in which two vicinal aromatic H-atoms at δ(H) 6.87 (*d*, $J=8.0$) and 6.50 (*d*, $J=8.0$ Hz) indicated four substituents. In the HMBC spectrum, the Me group at δ(H) 2.17 (*s*) showed correlations with C(3), C(4), and C(5), and the signal at δ(H) 6.87 (*d*, $J=8.0$ Hz) showed correlations with C(1), C(5), and the Me group at δ(C) 19.3 (*q*). Thus, the Me and OH groups were located at C(4) and C(1), respectively. On the basis of similar NOE correlations, the relative configurations of rings *B*–*D* were assumed to be the same as in **1**. From these data, the structure of **2** was secured. Note that this is the first report of a 19-norpregnane steroid from this soft coral.

The molecular formula of **3** was established as $C_{21}H_{32}O_2$, according to HR-FAB-MS (*m*/*z* 317.2475 ($[M+1]^+$; calc. 317.2481) and NMR analysis. The NMR data were characteristic of a pregnane-type steroid resembling pregna-1,20-dien-3-one [18]. 2D-NMR Spectroscopic analysis and comparison of the NMR data with those of known analogues [18] led to the identification of **3** as (5α)-20-hydroxypregn-1-en-3-one.

The ^{1}H-NMR spectrum of **3** displayed two Me groups at δ(H) 0.72 (*s*, Me(18)) and 1.03 (*s*, Me(19)), as well as two coupled olefinic H-atoms at δ(H) 7.16, 5.88 (2*d*, $J=10.5$ Hz each). These signals, in combination with the resonances at δ(C) 200.3 (*s*), 127.3 (*d*), and 158.5 (*d*), were attributable to the enone unit of ring *A*, closely related to those of pregna-1,20-dien-3-one [18]. The difference between the two compounds was in the side chain, the vinyl group at C(17) being hydrated in compound **3**, as confirmed by

Table 2. *^{13}C-NMR Data of* **1**–**4**. At 125 MHz in $CDCl_3$; δ in ppm.

Position	**1**	**2**	**3**	**4**
1	61.6 (*d*)	152.9 (*s*)	158.5 (*d*)	157.1 (*d*)
2	76.6 (*d*)	112.8 (*d*)	127.3 (*d*)	127.3 (*d*)
3	205.0 (*s*)	127.4 (*d*)	200.3 (*s*)	200.0 (*s*)
4	44.9 (*t*)	128.7 (*s*)	40.9 (*t*)	40.1 (*t*)
5	40.9 (*d*)	138.7 (*s*)	44.2 (*d*)	39.7 (*d*)
6	27.1 (*t*)	29.2 (*t*)	27.6 (*t*)	28.6 (*t*)
7	31.3 (*t*)	26.3 (*t*)	31.2 (*t*)	118.4 (*d*)
8	35.8 (*d*)	40.1 (*d*)	35.2 (*d*)	138.0 (*s*)
9	54.2 (*d*)	45.1 (*d*)	49.9 (*d*)	45.3 (*d*)
10	40.2 (*s*)	127.0 (*s*)	38.9 (*s*)	37.4 (*s*)
11	21.1 (*t*)	26.0 (*t*)	20.9 (*t*)	21.3 (*t*)
12	37.0 (*t*)	38.2 (*t*)	38.7 (*t*)	38.3 (*t*)
13	43.6 (*s*)	44.4 (*s*)	41.9 (*s*)	42.3 (*s*)
14	55.0 (*d*)	54.8 (*d*)	56.1 (*d*)	55.0 (*d*)
15	24.7 (*t*)	24.3 (*t*)	24.0 (*t*)	23.7 (*t*)
16	28.2 (*t*)	27.3 (*t*)	25.7 (*t*)	25.1 (*t*)
17	55.2 (*d*)	55.5 (*d*)	58.3 (*d*)	58.2 (*d*)
18	12.9 (*q*)	13.5 (*q*)	12.7 (*q*)	12.6 (*q*)
19	15.3 (*q*)	19.3 (*q*)	13.0 (*q*)	12.7 (*q*)
20	139.5 (*d*)	140.0 (*d*)	70.2 (*d*)	70.3 (*d*)
21	114.8 (*t*)	114.5 (*t*)	23.5 (*q*)	23.7 (*q*)
22	51.4 (*t*)	–	–	–

the presence of an additional Me signal at δ(H) 1.26 (*d*, $J = 6.0$ Hz), the corresponding coupled CH at δ(H) 3.74 (*dq*, $J = 6.0$, 7.5 Hz), and the respective C-atoms at δ(C) 23.5 (*q*, C(21)) and 70.2 (*d*, C(20)). HMBC Correlations from the Me H-atoms (δ(H) 1.26) to C(20) and C(17) (δ(C) 58.3 (*d*)) supported this. Although a NOESY experiment showed a correlation between H−C(20) and Me(19), the configuration at C(20) could not unequivocally be determined yet.

The ^{1}H-and ^{13}C-NMR data of **4** were very similar to those of **3**, with the exception of a molecular-weight difference of 2 amu and the presence of an additional C=C bond (δ(C) 118.4 (*d*), 138.0 (*s*); δ(H) 5.31 (br.)) in **4**. Further comparison of ^{13}C-NMR data revealed that the signals for C(7) and C(8) in **3** were absent in **4**. This suggested that the additional C=C bond was located at C(7). The signal of C(9) at δ(C) 45.3 (*d*) was shifted upfield and, in turn, its H-atom resonance (δ(H) 1.96–1.99 (*m*) was shifted downfield relative to those of **3**, which further supported Δ^7 unsaturation. Accordingly, the structure of **4** was determined as (5α)-20-hydroxypregna-1,7-dien-3-one.

This work was supported by grants from the *National High Technology Development Project* (project 863: No. 2001AA620403, 2003AA620403, and 2002AA217081; project 973: No. 2002CB41240), the *Chinese Academy of Science* (No. KJCX315-215), the *National Natural Science Foundation of China* (No. 40176038 and 30171106), and the International Cooperation Project of '2+2' (BMBF-MOST).

Experimental Part

General. Column chromatography (CC): silica gel (200–300 mesh; *Qingdao Marine Chemical Co., Ltd*., Qingdao, P. R. China) or *Sephadex LH-20* (18–110 μm; *Pharmacia*). Anal. TLC: *HF-254* silica gel (*Qingdao*). Optical rotations: *Perkin-Elmer 243B* polarimeter. IR Spectra: *Thermo Nicolet Nexus 470 FT-IR* spectrometer; in cm^{-1}. ^1H-, ^{13}C-, and 2D-NMR Spectra: *Bruker Avance-500X* and *Varian INOVA-500* spectrometers; chemical shifts δ in ppm rel. to residual solvent signals ($CHCl_3$: δ(H) 7.26, δ(C) 77.0 ppm), coupling constants *J* in Hz. HR-FAB-MS: *Bruker FTICR-APEXII* mass spectrometer; in *m*/*z*.

Animal Material. The soft corals *Cladiella krempfi* were collected by scuba diving in the inner reef of Hainan Island in November 2003. A voucher specimen (HSE-7A) was deposited at the State Key Laboratory of Natural and Biomimetic Drugs, Peking University, P. R. China. The animals were authenticated by Dr. *Leen van Ofwegen*, Institute of Systematic Population Biology, Amsterdam University, The Netherlands.

Extraction and Isolation. The soft corals (1.87 kg) were homogenized and then extracted with MeOH. The MeOH extract was concentrated under reduced pressure, and the residue (156 g) was successively partitioned between H_2O and petroleum ether (PE), AcOEt, and BuOH. The PE fraction (29.0 g) was subjected to CC (SiO_2; PE/acetone 50:1 → 1:1): 18 fractions, *Fr. 1–18*, according to TLC. *Fr. 5* (40 mg; eluted with PE/acetone 10:1), was separated by CC (*Sephadex LH-20*; H_2O/MeOH 10:90) to yield **1** (0.7 mg) and **2** (0.6 mg). *Fr. 7* (240 mg, eluted with PE/acetone 5:1) was resubjected to CC (SiO_2; PE/AcOEt 6:1) to afford **3** (2.0 mg) and **4** (8.0 mg).

Krempene A (=*(1*R*,3a*S*,3b*S*,5a*S*,7a*S*,11a*R*,11b*S*,11c*S*,13a*R*)-Hexadecahydro-1-ethenyl-11b,13a-dimethyl-7*H*-cyclopenta[7,8]phenanthro[4,3-*e*][1,3,4]oxadithiin-7-one*; **1**). Colorless, amorphous solid. $[\alpha]_D^{25} = +60.0$ (*c* = 0.6, MeOH). IR (KBr): 3020, 2924, 2851, 1700, 1639, 1550, 1447, 1383, 1189, 1040. ^1H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. HR-FAB-MS: 393.1916 ($[M+1]^+$, $C_{22}H_{33}O_2S_2$; calc. 393.1922).

Krempene B (=*4-Methyl-19-norpregna-1,3,5(10),20-tetraen-1-ol*; **2**). Colorless, amorphous solid. $[\alpha]_D^{25} = +82.9$ (*c* = 0.7, MeOH). IR (KBr): 3072, 2923, 2856, 1635, 1590, 1457, 1270, 1159, 1033. ^1H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. HR-EI-MS: 296.2132 (M^+, $C_{21}H_{28}O^+$; calc. 296.2140).

Krempene C (=*(5α)-20-Hydroxypregn-1-en-3-one*; **3**). Colorless, amorphous solid. $[\alpha]_D^{25} = +57.1$ (*c* = 0.3, MeOH). IR (KBr): 3456 (OH), 3031, 2931, 2868, 1675, 1447, 1376, 1262, 1153, 1109. ^1H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. HR-FAB-MS: 317.2475 ($[M+1]^+$, $C_{21}H_{33}O_2^+$; calc. 317.2481).

Krempene D (=*(5α)-20-Hydroxypregna-1,7-dien-3-one*; **4**). Colorless, amorphous solid. $[\alpha]_D^{25} = +11.7$ (*c* = 0.6, MeOH). IR (KBr): 3447 (OH), 2956, 2919, 2851, 1673, 1548, 1463, 1376, 1258, 1158, 1034. ^1H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. HR-FAB-MS: 315.2319 ($[M+1]^+$, $C_{21}H_{31}O_2^+$; calc. 315.2324).

REFERENCES

[1] C. A. Gray, M. T. Davies-Coleman, M. H. Schleyer, *J. Nat. Prod*. **2000**, *63*, 1551.
[2] N. S. Sarma, R. Chavakula, I. N. Rao, R. Kadirvelraj, T. N. G. Row, I. Saito, *J. Nat. Prod*. **1993**, *56*, 1977.
[3] R. Kazlauskas, P. T. Murphy, R. J. Wells, P. Schueholzer, *Tetrahedron Lett*. **1977**, *18*, 4643.
[4] J. E. Hochlowski, D. J. Faulkner, *Tetrahedron Lett*. **1980**, *21*, 4055.
[5] K. Yamada, N. Ogata, K. Ryu, T. Miyamoto, T. Komori, R. Higuchi, *J. Nat. Prod.* **1997**, *60*, 393.
[6] Y. Uchio, M. Nakatani, T. Hase, M. Kodama, S. Usui, Y. A. Fukazawa, *Tetrahedron Lett*. **1989**, *30*, 3331.
[7] Y. Uchio, M. Kodama, S. Usui, Y. Fukazawa, *Tetrahedron Lett*. **1992**, *33*, 1317.
[8] J.-K. Liu, L.-M. Zeng, D.-G. Wu, *Chin. Sci. Bull*. **1992**, *37*, 1627.
[9] K. Yamada, N. Ogata, K. Ryu, T. Miyamoto, T. Komori, R. Higuchi. *J. Nat. Prod*. **1997**, *60*, 393.
[10] C. B. Rao, D. S. Rao, C. Satyanaraayana, D.-V. Rao, K. E. Kassuhlke, D. J. Faulkner, *J. Nat. Prod.* **1994**, *57*, 574.
[11] J. Liu, L. Zeng, Y. Huang, *Zhongshan Daxue Xuebao, Ziran Kexueban* **1993**, *32*, 131.
[12] A. Ata, J. Ackerman, P. Radhika, *Tetrahedron Lett*. **2003**, *44*, 6951.

[13] M.-Y. Wang, Y. Luo, J.-Y. Su, *Chin. Chem. Lett.* **2000**, *11*, 783.
[14] N. S. Sarma, R. Chavakula, S. R. Rao, *Indian J. Chem., B* **1995**, *34*, 264.
[15] V. Anjaneyulu, P. V. Subba, P. Radhika, H. Laatsch, R. N. Asolkar, *Indian J. Chem., B* **2001**, *40*, 405.
[16] W. Lan, C.-W. Lin, J.-Y. Su, L.-M. Zeng, *Chem. J. Chin. Univ.* **2003**, *24*, 2019.
[17] G. Wang. Q. Liu, L. Zeng, *Zhongshan Daxue Xuebao, Ziran Kexueban* **1995**, *34*, 110.
[18] G.-W. Zhang, X. Ma, L. Zeng, J. Su, *Chin. J. Appl. Chem*. **2003**, *20*, 1021.
[19] X. Huang, Z. Deng, L. V. Ofwegen, J. Li, H. Fu, X. Zhu, W. Lin, *J. Asian Nat. Prod. Res.* **2006**, *8*, 287.
[20] C. L. Jennings-White, D. L. Berliner, N. W. Adams, to *Pherin Corp.*, PCT Int. Appl. No. US1996/009665.

Received May 23, 2006