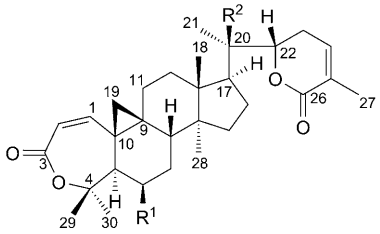
Two New Triterpenoids from the Stems of *Schisandra bicolor*

by **Wenhui Ma**[a]), **Jiancheng He**[b]), **Lin Li**[a]), and **Luping Qin***[a])

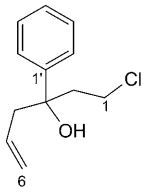
[a]) Department of Pharmacognosy, School of Pharmacy, Second Military Medical University, Shanghai 200433, P. R. China
(phone: +86-21-81871300; fax: +86-21-81871300; e-mail: qinsmmu@126.com)
[b]) Microscreen Biotechnology Co., Ltd., Shanghai 201203, P. R. China

Two new triterpenoids, schisanbilactones A and B (**1** and **2**, resp.), and a new natural product, 1-chloro-3-phenylhex-5-en-3-ol (**3**), as well as a known triterpenoid, kadsulactone A (**4**), were isolated from the stems of *Schisandra bicolor*. The structures of the new compounds were elucidated by spectroscopic analyses, including 2D-NMR techniques.

Introduction. – Plants of the family Schisandraceae have proved to be a rich source of dibenzocyclooctane lignans, as well as lanostane and cycloartane triterpenes, which have been found to possess many beneficial pharmacological effects, such as anti-lipid peroxidative, antitumor, and anti-HIV activities [1–5]. In our previous study, four new lignans and three new carotane sesquiterpenoids were isolated from the stems of *Kadsura induta* and *Schisandra wilsoniana*, and some of them were found to show an antiviral effect against the hepatitis B virus [6–8]. In the course of searching for new bioactive natural products from Schisandraceae plants, two new triterpenoids, schisanbilactones A and B (**1** and **2**, resp.), and a new natural product, 1-chloro-3-phenylhex-5-en-3-ol (**3**), as well as a known triterpenoid, kadsulactone A (**4**), were isolated from the stems of *Schisandra bicolor* CHENG, indigenous to southern China. This article describes the isolation and the structural elucidation of the new compounds.



1 R^1 = AcO, R^2 = H
2 R^1 = OH, R^2 = OH
4 R^1 = OH, R^2 = H



3

Results and Discussion. – Repeated column chromatography of the Et_2O extract from the stems of *S. bicolor* yielded compounds **1**–**4**.

Schisanbilactone A (**1**) was obtained as a white powder and was shown to possess the molecular formula $C_{32}H_{44}O_6$ on the basis of HR-ESI-MS (*m/z* 547.3044 ($[M+Na]^+$)), which indicated eleven degrees of unsaturation. The IR spectrum indicated the presence of a six-membered α,β-unsaturated lactone (1718 cm^{-1}) and a seven-membered α,β-unsaturated lactone (1685 cm^{-1}) [9].

The ^{1}H-NMR spectrum (*Table 1*) showed a secondary Me group (δ(H) 0.97, *d*, *J* = 6.4) and six tertiary Me groups (δ(H) 0.92, 1.01, 1.41, 1.47, 1.90, and 2.03, 6*s*). As determined by DEPT experiment, the down-field signals corresponded to three CO groups (δ(C) 166.5, 166.8, and 169.6), four olefinic (δ(C) 119.8, 128.3, 139.4, and 150.7), and three O-bearing C-atoms (δ(C) 70.5, 80.4, and 83.6); the shielded region showed seven Me (δ(C) 13.1, 17.0, 18.0, 19.5, 21.2, 23.9, and 27.9), seven CH_2 (δ(C) 23.4, 26.9, 28.5, 28.8, 32.4, 35.8, and 36.5), and four CH groups (δ(C) 39.1, 40.7, 48.1, and 48.2), as well as four quaternary C-atoms (δ(C) 27.9, 32.0, 45.6, and 47.7) (*Table 2*). The NMR spectra of **1** were very similar to those of kadsulactone A (**4**), suggesting that **1** has the same skeleton as **4**.

Table 1. *^{1}H-NMR Data of* **1** *and* **2** (at 400 MHz, in $CDCl_3$ at 27°; δ in ppm, *J* in Hz).

	1	**2**
H–C(1)	6.03 (*d*, *J* = 12.7)	6.03 (*d*, *J* = 12.8)
H–C(2)	5.90 (*d*, *J* = 12.7)	5.89 (*d*, *J* = 12.8)
H–C(5)	2.53 (*d*, *J* = 3.6)	2.32 (*d*, *J* = 3.6)
H–C(6)	5.27–5.33 (*m*)	4.44–4.48 (*m*)
CH_2(7)	1.33–1.41 (*m*), 1.70–1.78 (*m*)	1.42–1.49 (*m*), 1.75–1.83 (*m*)
H–C(8)	1.77–1.85 (*m*)	2.18–2.26 (*m*)
CH_2(11)	1.38–1.45 (*m*), 2.16–2.28 (*m*)	1.42–1.50 (*m*), 2.22–2.30 (*m*)
CH_2(12)	1.67–1.80 (*m*)	1.78–1.86 (*m*)
CH_2(15)	1.21–1.26 (*m*), 1.30–1.36 (*m*)	1.33–1.41 (*m*), 1.40–1.48 (*m*)
CH_2(16)	1.40–1.53 (*m*), 1.75–1.84 (*m*)	1.55–1.63 (*m*), 1.96–2.03 (*m*)
H–C(17)	1.56–1.65 (*m*)	1.93–2.01 (*m*)
Me(18)	1.01 (*s*)	1.26 (*s*)
CH_2(19)	1.23 (*d*, *J* = 4.5), 1.73 (*d*, *J* = 4.5)	1.17 (*d*, *J* = 4.3), 1.97 (*d*, *J* = 4.3)
H–C(20)	1.96–2.04 (*m*)	–
Me(21)	0.97 (*d*, *J* = 6.4)	1.32 (*s*)
H–C(22)	4.44 (*dq*, *J* = 7.6, 13.2)	4.29 (*dd*, *J* = 4.5, 12.8)
CH_2(23)	1.95–2.07 (*m*)	2.26–2.33 (*m*)
H–C(24)	6.59 (*d*, *J* = 6.4)	6.60 (*d*, *J* = 6.0)
Me(27)	1.90 (*s*)	1.93 (*s*)
Me(28)	0.92 (*s*)	0.97 (*s*)
Me(29)	1.47 (*s*)	1.67 (*s*)
Me(30)	1.41 (*s*)	1.50 (*s*)
AcO	2.03 (*s*)	–

Comparison of the NMR spectra of **1** and **4** showed that the OH group at C(6) in **4** was replaced by an AcO group in **1**. The fragment ion at *m/z* 43 ($C_2H_3O^+$) in the EI-MS of **1** suggested the presence of an AcO group, as confirmed by the NMR signals at δ(H) 2.03 (*s*), and δ(C) 169.6 and 21.2. The HMBC correlations (*Fig. 1*) of δ(H) 5.27–5.33 (H–C(6)) with δ(C) 169.6 (C=O) revealed that the AcO group is located at C(6).

Table 2. *^{13}C-NMR Data of* **1**, **2**, *and* **4** (at 100 MHz, in $CDCl_3$ at 27°; δ in ppm)

	1	**2**	**4**
1	150.7 (*d*)	151.7 (*d*)	151.9 (*d*)
2	119.8 (*d*)	119.4 (*d*)	119.3 (*d*)
3	166.8 (*s*)	167.6 (*s*)	167.6 (*s*)
4	83.6 (*s*)	84.8 (*s*)	84.9 (*s*)
5	48.2 (*d*)	48.8 (*d*)	48.8 (*d*)
6	70.5 (*d*)	66.7 (*d*)	66.5 (*d*)
7	26.9 (*t*)	33.3 (*t*)	33.2 (*t*)
8	40.7 (*d*)	39.1 (*d*)	39.6 (*d*)
9	27.9 (*s*)	27.8 (*s*)	28.0 (*s*)
10	32.0 (*s*)	32.0 (*s*)	32.0 (*s*)
11	28.5 (*t*)	28.8 (*t*)	27.1 (*t*)
12	32.4 (*t*)	33.2 (*t*)	32.6 (*t*)
13	47.7 (*s*)	48.2 (*s*)	47.9 (*s*)
14	45.6 (*s*)	46.3 (*s*)	45.7 (*s*)
15	35.8 (*t*)	35.3 (*t*)	35.7 (*t*)
16	28.8 (*t*)	21.7 (*t*)	28.7 (*t*)
17	48.1 (*d*)	50.9 (*d*)	48.3 (*d*)
18	18.0 (*q*)	20.1 (*q*)	18.2 (*q*)
19	36.5 (*t*)	37.4 (*t*)	37.2 (*t*)
20	39.1 (*d*)	75.4 (*s*)	39.1 (*d*)
21	13.1 (*q*)	20.7 (*q*)	13.1 (*q*)
22	80.4 (*d*)	83.1 (*d*)	80.5 (*t*)
23	23.4 (*t*)	25.6 (*t*)	23.5 (*t*)
24	139.4 (*d*)	139.0 (*d*)	139.5 (*d*)
25	128.3 (*s*)	128.3 (*s*)	128.3 (*s*)
26	166.5 (*s*)	165.5 (*s*)	166.6 (*s*)
27	17.0 (*q*)	16.9 (*q*)	17.0 (*q*)
28	19.5 (*q*)	19.9 (*q*)	19.7 (*q*)
29	27.9 (*q*)	28.1 (*q*)	28.1 (*q*)
30	23.9 (*q*)	24.0 (*q*)	24.0 (*q*)
AcO	169.6 (*s*), 21.2 (*q*)	–	–

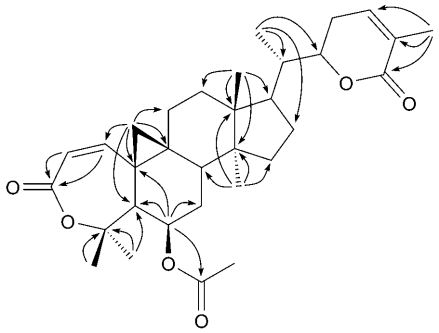


Fig. 1. *Key HMBCs in* **1**

Compound **1** was inferred to have (*S*)-configuration at C(22) on the basis of a negative *Cotton* effect at 240 nm and a positive *Cotton* effect at 281 nm, similar to those of **4** [9].

Schisanbilactone B (**2**), obtained as a white powder, had the molecular formula $C_{30}H_{42}O_6$ with ten degrees of unsaturation determined by HR-ESI-MS (*m/z* 521.2884 ($[M+Na]^+$)). The IR spectrum showed the presence of a OH group (3434 cm^{-1}). The NMR, IR, and UV spectra of **2** were very similar to those of kadsulactone A (**4**), indicating that **2** also has the same skeleton as **4**. The ^{1}H-NMR spectrum (*Table 1*) showed six tertiary Me groups (δ(H) 0.97, 1.26, 1.32, 1.50, 1.67, and 1.93, 6*s*). Comparison of the ^{1}H-NMR spectra of **2** and **4** showed that the secondary Me signal present in the latter at δ(H) 0.98 (*d*, $J=6.4$, Me(21)) had disappeared in **2**, instead appearing as a tertiary Me signal at δ(H) 1.32. HMBCs between Me(21) at δ(H) 1.32 and C(17) at δ(C) 50.9, C(20) at δ(C) 75.4, and C(22) at δ(C) 83.1, indicated a OH group at C(20), similar as renchanglactone A [10]. The CD spectrum of **2** showed a negative *Cotton* effect at 237 nm and a positive effect at 281 nm, which indicated that **2** had (*S*)-configuration at C(22) similar to that of **1**, different from that of renchanglactone A [10].

Compound **3**, a colorless, optically active oil, had the molecular formula $C_{12}H_{15}ClO$ according to HR-EI-MS (*m/z* 169.0417 ($[M-CH_2CH{=}CH_2]^+$)). The IR spectrum showed the presence of a OH group (3448 cm^{-1}). The ^{1}H-NMR signals at δ(H) 5.51–5.62 (*m*, 1 H), 5.18–5.20 (*m*, 2 H), and ^{13}C-NMR signals at δ(C) 120.6 and 132.5, suggested a monosubstituted C=C bond in **3**. The fragment ion at *m/z* 41 and NMR signals, along with a HMBC (*Fig. 2*) of CH_2(6) at δ(H) 5.18–5.20 to C(4) at δ(C) 47.8, indicated the presence of a $CH_2CH{=}CH_2$ group. The fragment ions at *m/z* 91 ($C_7H_7^+$), 77 ($C_6H_5^+$), and 51 ($C_4H_3^+$), as well as NMR signals (*Table 3*), suggested a monosubstituted Ph group in **3**. The HMBC between H–C(2′) and H–C(6′) and

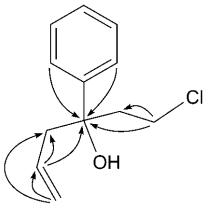


Fig. 2. *Key HMBCs in* **3**

Table 3. *^{1}H- and ^{13}C-NMR Data of* **3** (at 400 and 100 MHz, resp., in $CDCl_3$ at 27°; δ in ppm, *J* in Hz)

	δ(H)	δ(C)
CH_2(1)	3.20–3.29 (*m*), 3.56–3.65 (*m*)	40.2 (*t*)
CH_2(2)	2.32–2.38 (*m*)	45.5 (*t*)
C(3)	–	75.2 (*s*)
CH_2(4)	3.20–3.29 (*m*), 3.56–3.65 (*m*)	47.8 (*t*)
H–C(5)	5.51–5.62 (*m*)	132.5 (*d*)
CH_2(6)	5.18–5.20 (*m*)	120.6 (*t*)
C(1′)	–	144.4 (*s*)
H–C(2′,6′)	7.36–7.45 (*m*)	128.5 (*d*)
H–C(3′,5′)	7.36–7.45 (*m*)	125.0 (*d*)
H–C(4′)	7.27–7.33 (*m*)	127.0 (*d*)
OH	2.28 (*s*)	

C(3) at δ(C) 75.2 indicated that the Ph group was connected to C(3). Finally, the structure of **3** was elucidated as 1-chloro-3-phenylhex-5-en-3-ol of as yet unknown absolute configuration, based on the HSQC and HMBC spectra.

Experimental Part

General. Anal. TLC was performed on silica-gel plates (*Yan-tai Institute of Chemical Technology*), with petroleum ether (PE)/acetone 3:1 as eluent; visualization under UV light, and by spraying with 10% aq. H_2SO_4, followed by heating. Column chromatography (CC): silica gel (SiO_2; 200–300, or 300–400 mesh; *Qingdao Marine Chemical Factory*). Optical rotations (ORD): *JASCO P-1020* spectropolarimeter. UV Spectra: *Shimadzu UV-260* spectrophotometer, in anh. MeOH; λ_{max} (log ε) in nm. CD Spectra: *JASCO J-715* spectropolarimeter; λ in nm ($\Delta\varepsilon$). IR Spectra: *Avatar 360-ESP* spectrophotometer (*Thermo Nicolet*), as KBr pellets; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *DRX-400* spectrometer, in $CDCl_3$; δ in ppm, J in Hz. EI-MS: *Agilent 5973N* mass spectrometer; in *m/z* (rel. %). HR-ESI-MS: *Bruker APEX 7.0 TESLA FT-MS* apparatus. HR-EI-MS: *Waters Micromass GCT.*

Plant Material. The stems of *Schisandra bicolor* were collected at Tianmu mountain, Zhejiang Province, P. R. China, in June 2008. A voucher specimen (Qin-Ma200801) is deposited at the Herbarium of Materia Medica, School of Pharmacy, the Second Military Medical University, Shanghai, P. R. China.

Extraction and Isolation. The air-dried, ground stems (3 kg) of *S. bicolor* were extracted exhaustively with 95% aq. EtOH at r.t. The EtOH extract was concentrated *in vacuo* to yield a semi-solid (400 g), which was suspended in H_2O (400 ml), and extracted with Et_2O (3 × 400 ml). The combined org. phases were concentrated to yield a residue (100 g), part of which (95 g) was subjected to CC (2 kg of SiO_2; PE/AcOEt gradient) to afford seven fractions (*Frs. 1–7*). *Fr. 5*, eluted with PE/AcOEt 3:1, was subjected to repeated CC (SiO_2; PE/AcOEt 5:1), and then with PTLC (PE/AcOEt 5:3) to afford **1** (10 mg), **4** (36 mg), and **3** (10 mg). *Fr. 5*, eluted with PE/AcOEt 1:1, was subjected to repeated CC (SiO_2; PE/AcOEt 2:1), and then with PTLC (PE/acetone 3:2) to afford **2** (16 mg).

Schisanbilactone A (= *(1*R*,3a*S*,5*R*,10a*S*,11a*S*,13a*R*)-1,2,3,3a,3b,4,5,5a,6,12,13,13a-Dodecahydro-3a,6,6,13a-tetramethyl-1-[(1*S*)-1-((2*S*)-5-methyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)ethyl]-8-oxo-8*H*-cyclopenta[5,6]cyclopropa[1,8a]naphtho[2,1-c]oxepin-5-yl Acetate*; **1**). White powder. $[\alpha]_D^{25} = +72$ (c = 0.05, MeOH). UV (MeOH): 206 (4.18), 249 (4.26). CD (c = 0.01, MeOH): 240 (−4.5), 257 (−5.0), 281 (+32.2). IR (KBr): 2943, 1718, 1685, 1466, 1388, 1235, 1119, 1030. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. EI-MS: 446 (7), 169 (45), 107 (55), 105 (68), 95 (74), 93 (55), 91 (63), 55 (77), 43 (100). HR-ESI-MS: 547.3044 ($[M+Na]^+$, $C_{32}H_{44}NaO_6^+$; calc. 547.3031).

Schisanbilactone B (= *(1*S*,3a*S*,5*R*,10a*S*,11a*S*,13a*R*)-1,2,3,3a,3b,4,5,5a,6,12,13,13a-Dodecahydro-5-hydroxy-1-[(1*R*)-1-hydroxy-1-((2*S*)-5-methyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)ethyl]-3a,6,6,13a-tetramethyl-8*H*-cyclopenta[5,6]cyclopropa[1,8a]naphtho[2,1-c]oxepin-8-one*; **2**). White powder. $[\alpha]_D^{25} = +68$ (c = 0.05, MeOH). UV (MeOH): 206 (4.35), 252 (4.35). CD (c = 0.01, MeOH): 237 (−6.8), 281 (+28.1). IR (KBr): 3434, 2925, 1718, 1663, 1383, 1121, 915. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. EI-MS: 117 (19), 105 (12), 104 (100), 103 (50), 91 (79), 78 (40), 77 (24), 51 (22). ESI-MS: 415.1 ($[M+H]^+$). HR-ESI-MS: 521.2884 ($[M+Na]^+$, $C_{30}H_{42}NaO_6^+$; calc. 521.2874).

1-Chloro-3-phenylhex-5-en-3-ol (**3**). Colorless oil. $[\alpha]_D^{25} = +4.2$ (c = 0.04, MeOH). IR (KBr): 3448, 2926, 2366, 2345, 1654, 1638, 1447, 1060, 923, 702. ^{1}H- and ^{13}C-NMR: *Table 3*. EI-MS: 171 (34), 170 (11), 169 (100), 105 (88), 93 (12), 91 (43), 77 (42), 63 (17), 41 (6). HR-EI-MS: 169.0417 ($[M-CH_2CH{=}CH_2]^+$, $C_9H_{10}ClO^+$; calc. 169.0420).

REFERENCES

[1] X.-W.Yang, M. Hattori, T. Namba, D.-F. Chen, G.-J. Xu, *Chem. Pharm. Bull.* **1992**, *40*, 406.
[2] L.-J. Xu, F. Huang, S.-B. Chen, Q.-X. Zhang, L.-N. Li, S.-L. Chen, P.-G. Xiao, *Planta Med.* **2006**, *72*, 169.
[3] M. Chen, N. Kilgore, K.-H. Lee, D.-F. Chen, *J. Nat. Prod.* **2006**, *69*, 1697.

[4] D.-F. Chen, S.-X. Zhang, H.-K. Wang, S.-Y. Zhang, Q.-Z. Sun, L. M. Cosentino, K.-H. Lee, *J. Nat. Prod.* **1999**, *62*, 94.
[5] Y.-H. Kuo, H.-C. Huang, L.-M. Y. Kuo, C.-F. Chen, *J. Org. Chem.* **1999**, *64*, 7023.
[6] W. Ma, X. Ma, H. Huang, P. Zhou, D. Chen, *Chem. Biodiversity* **2007**, *4*, 966.
[7] W. Ma, X. Ma, Y. Lu, D. Chen, *Helv. Chim. Acta* **2009**, *92*, 709.
[8] W.-H. Ma, H. Huang, P. Zhou, D.-F. Chen, *J. Nat. Prod.* **2009**, *72*, 676.
[9] Y. Chen, Z. Lin, H. Zhong, H. Sun, *Phytochemistry* **1990**, *29*, 3358.
[10] M. Chen, D.-F. Cheng, *Nat. Prod. Res.* **2008**, *22*, 203.

Received June 29, 2009