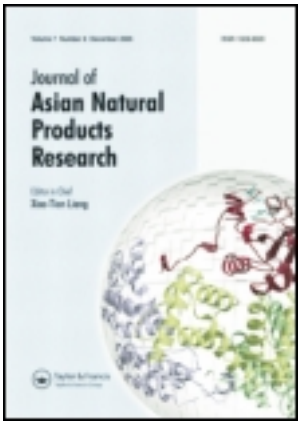

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Dibenzocyclooctadiene lignans from the fruits of *Schisandra rubriflora* and their anti-HIV-1 activities

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Two new dibenzocyclooctadiene lignans, rubrilignans A and B (**1**, **2**), together with 17 known ones, were isolated from the fruits of *Schisandra rubriflora*. The structures of **1** and **2** were elucidated by spectroscopic methods including extensive 1D and 2D NMR techniques. Compounds **1** and **2** were also evaluated for their anti-HIV-1 activities and showed weak anti-HIV-1 activity with EC_{50} values of 2.26 and 1.82 μg/ml, and therapeutic index values of 35.5 and 18.6, respectively.

Keywords: Schisandreae; *Schisandra rubriflora*; fruits; dibenzocyclooctadiene lignans; anti-HIV-1 activity

1. Introduction

Plants of the economically and medicinally important genus *Schisandra* (Schisandreae) are known to be a rich source of dibenzocyclooctadiene lignans, lanostane, and cycloartane triterpenes, and more than 19 species are widely used as sedative and tonic agents in traditional Chinese medicine [1–3]. Since 2003, the systematical chemical investigation of the genus *Schisandra* conducted by our group led to the discovery of a series of novel nortriterpenoids with a diversity of highly oxygenated structures biogenetically related to cycloartane, some of which showed promising anti-HIV-1 activities with low toxicities [3–6].

Schisandra rubriflora A. C. Smith belongs to the genus *Schisandra* of the family Schisandraceae, which is widely distributed in mainland China. In previous work, some bioactive compounds, including new highly oxygenated nortriterpenoids, carotane sesquiterpenoids, and lignans, were isolated from this plant [2,3,7–10]. Motivated by a search for bioactive metabolites from this plant, a reinvestigation on the chemical constituents of the fruits of *S. rubriflora* was carried out. As a result, 19 dibenzocyclooctadiene lignans were isolated, including two new lignans, rubrilignans A and B (**1**, **2**). In addition, the anti-HIV-1 activities of compounds **1** and **2** were evaluated. This article deals with the isolation, structural elucidation, and biological activities of the two new compounds.

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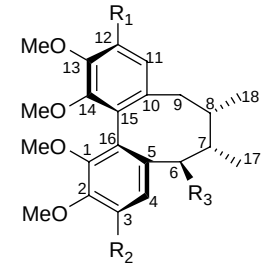
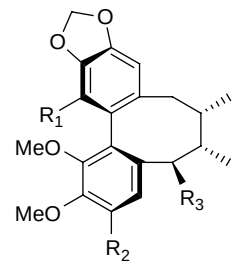
2. Results and discussion

Air-dried and powdered fruits (1.7 kg) were extracted with 70% aqueous Me_2CO (3 × 2.5 L) at room temperature and filtered to yield a filtrate that was successively evaporated under reduced pressure and partitioned with EtOAc. The EtOAc portion (52 g) was subjected to column chromatography on silica gel, Sephadex LH-20, RP-18, and preparative HPLC to afford compounds **1**–**19**, including two new lignans named rubrilignans A and B (**1**, **2**), together with 17 known lignans, marlignans G (3) [11], schisandrin A (**4**) [2], gomisin J (**5**) [2], wilsonilignan C (**6**) [12], rubschizantherin (**7**) [13], isogomisin O (**8**) [2], gomisin N (**9**) [2], gomisin S (**10**) [14], benzoylgomisin Q (**11**) [15], angeloygomisin Q (**12**) [2], gomisin Q (**13**) [2], gomisin C (**14**) [16], gomisin B (**15**) [16], marlignan L (**16**) [11], gomisin T (**17**) [14] schizandrin (**18**) [17], and (+)-gomisin K (**19**) [2]. The structures of the compounds **1**–**19** were shown in Figure 1, and ^{13}C-NMR spectroscopic data of **1** and **2** are listed in Table 1.

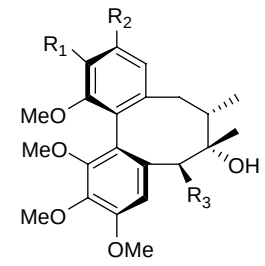
Compound **1** was obtained as yellow gum. Its molecular formula was determined as $C_{26}H_{34}O_8$ by its HRESIMS at *m/z* 475.2337 $[M + H]^+$. Its ^{1}H and ^{13}C NMR spectra showed the signals of 34 protons

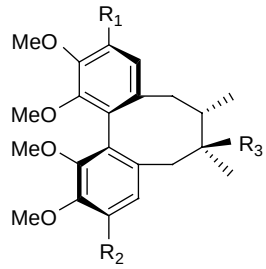




1 $R_1 = R_3 = OMe$; $R_2 = OAc$
2 $R_1 = OAc$; $R_2 = R_3 = OMe$
3 $R_1 = R_2 = OH$; $R_3 = OMe$
4 $R_1 = R_2 = OMe$; $R_3 = H$
5 $R_1 = R_3 = H$; $R_2 = OMe$

6 $R_1 = OH$; $R_2 = R_3 = OMe$
7 $R_1 = R_2 = OMe$; $R_3 = OAc$
8 $R_1 = R_2 = OMe$; $R_3 = OH$
9 $R_1 = R_2 = OMe$; $R_3 = H$
10 $R_1 = OMe$; $R_2 = R_3 = OH$





11 $R_1 = R_2 = OMe$; $R_3 = OBz$
12 $R_1 = R_2 = OMe$; $R_3 = OAng$
13 $R_1 = R_2 = OMe$; $R_3 = OH$
14 $R_1 = R_2 = OCH_2O$; $R_3 = OBz$
15 $R_1 = R_2 = OCH_2O$; $R_3 = OAng$

16 $R_1 = R_2 = OH$; $R_3 = OH$
17 $R_1 = R_3 = OH$; $R_2 = OMe$
18 $R_1 = R_2 = OMe$; $R_3 = OH$
19 $R_1 = OAc$; R_2 OMe; $R_3 = H$

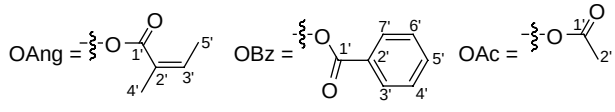


Figure 1. The structures of compounds **1**–**19**.

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** in $CDCl_3$ medium (δ in ppm).

	Compound **1**		Compound **2**	
No.	^{13}C (mult)	^{1}H (mult, J in Hz)	^{13}C (mult)	^{1}H (mult, J in Hz)
1	151.3 s		151.9 s	
2	142.7 s		141.7 s	
3	143.2 s		150.5 s	
4	116.8 d	6.72 s	111.4 d	6.52 s
5	133.6 s		133.7 s	
6	90.3 d	3.99, d, $J = 8.6$	90.4 d	3.96, d, $J = 8.6$
7	38.6 d	1.87 m	38.5 d	1.72 m
8	36.4 d	1.90 m	36.6 d	1.83 m
9	37.5 t	2.02, d, $J = 11.9$	37.8 t	1.97, d, $J = 10.7$
		2.34 m		2.32, m
10	136.6 s		136.8 s	
11	106.2 d	6.48 s	113.8 d	6.79 s
12	151.9 s		143.9 s	
13	140.5 s		143.2 s	
14	152.8 s		151.3 s	
15	122.5 s		121.7 s	
16	123.9 s		123.0 s	
17	17.5 q	0.92 overlap	17.4 q	0.86, d, $J = 8.5$
18	17.5 q	0.93 overlap	17.5 q	0.89, d, $J = 8.5$
1-OMe	60.3 q	3.90 s	59.9 q	3.85 s
2-OMe	60.8 q	3.89 s	60.9 q	3.88 s
3-OMe			56.0 q	3.91 s
12-OMe	56.0 q	3.95 s		
13-OMe	60.7 q	3.94 s	60.7 q	3.91 s
14-OMe	60.5 q	3.78 s	60.3 q	3.76 s
6-OMe	55.8 q	3.05 s	55.8 q	3.02 s
1'	169.4 s		169.3 s	
2'	21.5 q	1.97 s	21.3 q	2.02 s

and 26 carbons, respectively, corresponding to two aromatic rings (δ_C 106.2–152.8) with two aromatic protons (δ_H 6.48, 6.72), one methylene carbon (δ_C 37.5), two methine carbons (δ_C 36.4, 38.6), one oxidated methine carbon (δ_C 90.3), two methyl groups (δ_C 17.5, 17.5), six methoxy groups (δ_C 55.8, 56.0, 60.3, 60.5, 60.7, 60.8), and one acetoxy group (δ_C 21.5, 169.4), suggesting the presence of a biphenyl moiety [16]. In addition, the HMBC correlations of H-4 (δ_H 6.72) with C-5 (δ_C 133.6), C-6 (δ_C 90.3), and C-16 (δ_C 123.9), and of H-11 (δ_H 6.48) with C-9 (δ_C 37.5), C-10 (δ_C 136.6), and C-15 (δ_C 122.5), and $^{1}H-^{1}H$ COSY correlations of H-6/H-7/H-8/H-9, H-7/H-17, and H-8/H-18 (Figure 2), and UV absorption bands at 212, 252, 318 nm implied that **1** could be a dibenzocyclooctadiene lignan [16]. In the cyclooctadiene ring, two secondary methyl groups (δ_H 0.92 overlap, 0.93 overlap) can

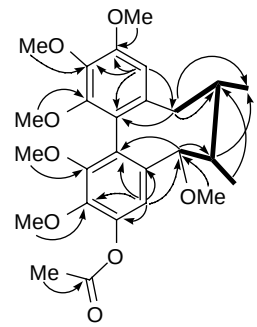


Figure 2. Selected HMBC (→) and $^{1}H-^{1}H$ COSY (–) correlations of **1**.

be assigned to CH_3-17 and CH_3-18, the methylene can be assigned to C-9, the oxidated methine can be assigned to C-6, and two methines can be assigned to C-7 and C-8 by the analysis of HMBC and $^1H-^1H$ COSY correlations (Figure 2). The methoxy proton signal at δ_H 3.05 and the chemical shift of C-6 (δ_C 90.3) indicated that a methoxy group was attached to C-6 [18], which was further confirmed by HMBC correlation of this methoxy (δ_H 3.05) with C-6. The chemical shift of the methoxy groups (δ_C 60.3, 60.5, 60.7, 60.8) suggested that the four methoxy groups were located at C-1, C-14, C-13, and C-2 in the aromatic rings [18], which was confirmed by HMBC correlations of the proton signals of δ_H 3.90 with C-1 (δ_C 151.3), δ_H 3.89 with C-2 (δ_C 142.7), δ_H 3.94 with C-13 (δ_C 140.5), and δ_H 3.78 with C-14 (δ_C 152.8). The HMBC correlation of another methoxy proton at δ_H 3.95 with C-12 and the ROESY correlation of the protons of this methoxy group with H-11 determined that this methoxy group was located at C-12 (Figure 2), and accordingly, the acetoxy group located at C-3 was deduced. The acetoxy group at C-3 was also supported by the chemical shift of C-3 down shift to 143.2 ppm, and HMBC correlation observed from H-4 with C-3.

As the CD spectrum of dibenzocyclooctadiene lignan was dominated by the axial chirality of the biphenyl chromophore, the absolute configuration of biphenyl axis was determined by the CD spectrum. The CD curve showed a negative Cotton effect around 250 nm and a positive one around 220 nm, suggesting that **1** possessed an *S*-biphenyl configuration [16]. With the axial chirality defined, a ROESY experiment was used to establish the relative configuration of the remaining stereocenters (Figure 3). The observed ROESY correlations of H-11 with H-9, H-4 with CH_3-17, and H-9 with CH_3-18 were consistent with a cyclooctadiene lignan with a twisted boat/chair conformation and the relative configurations of C-7 (*S*) and C-8 (*R*) (Figure 3) [19]. The configuration of 6-OMe was deduced as β-orientation by the chemical shift of C-6 (δ_C 90.3), which was similar to that of the 6-β-oriented derivatives of gomisins [18] and was distinct from that of 6-α-oriented components in dibenzocyclooctadiene lignan family [14,15]. Thus, the structure of **1** was established as shown in Figure 1, and given the name as rubrilignan A.

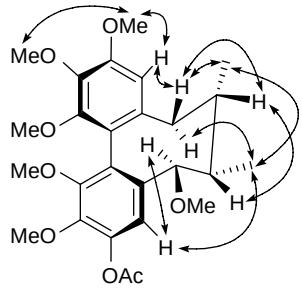


Figure 3. Key ROESY correlations (↔) of **1**.

Compound **2**, obtained as yellow gum, showed a quasi-molecular weight of 475.2327 $[M + H]^+$ in HRESIMS, corresponding to the molecular formula $C_{26}H_{34}O_8$. It showed absorption maxima in the UV spectrum at 210, 252, 316 nm. Its ^1H and ^{13}C NMR spectra showed the signals of 34 protons and 26 carbons. The ^1H and ^{13}C NMR spectra of **2** were very similar to those of **1**. The obvious chemical-shift differences resulted from the substituent groups in aromatic rings. Analysis of HSQC and HMBC spectra of **2** showed that the acetoxy group was attached to C-12 and the six methoxy groups were located at C-1, C-2, C-3, C-6, C-13, and C-14. Thus, the structure of **2** was also established, and given the name as rubrilignan B.

As some of dibenzocyclooctadiene lignans from the species of the *Schisandra* genus exhibited modest or strong anti-HIV activities, new compounds **1**–**2** were tested for their potencies in preventing the cytopathic effects of HIV-1 in C8166 and cytotoxicity was measured in parallel with the determination of antiviral activity, using azidothymidine as a positive control

(0.0043 μg/ml and $CC_{50} > 200$ μg/ml) [20]. Compounds **1** and **2** showed weak anti-HIV-1 activity with EC_{50} values of 2.26 and 1.82 μg/ml, and therapeutic index (TI) values of 35.5, 18.6, respectively.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. CD spectra were measured on a JASCO J-810 spectropolarimeter. A Tenor 27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. 1D and 2D NMR spectra were recorded on DRX-500 spectrometers with TMS as internal standard. Unless otherwise indicated, chemical shifts (δ) were expressed in ppm with reference to the solvent signals. HRESIMS were performed on a VG Autospec-3000 spectrometer. Preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatography with a ZORBAX PrepHT GF (21.2 mm × 25 cm) column or a Venusil MP C_{18} (20 mm × 25 cm) column. Column chromatography was performed with silica gel (200–300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany), and MCI gel (75–150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). The fractions were monitored by TLC, and spots were visualized by heating Si gel plates sprayed with 5% H_2SO_4 in EtOH.

3.2 Plant material

The fruits of *S. rubriflora* were collected in Dali Prefecture of Yunnan Province, China, in July 2007. The identification of plant material was verified by Prof. Xi-Wen Li. A voucher specimen (KIB 07-9-11) has been deposited in the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, China.

3.3 Extraction and isolation

The air-dried and powdered fruits of *S. rubriflora* (1.7 kg) were extracted with 70% aqueous Me_2CO (3 × 2.5 L) at room temperature and filtered to yield a filtrate that was successively evaporated under reduced pressure to obtain a crude extract (195 g). This crude extract was partitioned with EtOAc (3 × 2.5 L). The EtOAc partition (52 g) was applied to silica gel 200–300 mesh) column chromatography eluting with a $CHCl_3$–Me_2CO gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5) to give six fractions A–G. The separation of fraction A (12.5 g) by silica gel column chromatography eluted with petroleum ether–Me_2CO (20:1, 9:1, 8:2, 7:3, 2:1) yielded mixtures A1–A5. Fraction A2 (2.8 g) was subjected to silica gel column chromatography using petroleum ether–Me_2CO (9:1) and preparative HPLC (78% MeOH–H_2O, flow rate 12 ml/min) to give **1** (8.2 mg), **2** (11.5 mg), and **7** (52.8 mg). Fraction A3 (1.2 g) was subjected to silica gel column chromatography using petroleum ether–Me_2CO (8:2) and preparative HPLC (74% MeOH–H_2O, flow rate 12 ml/min) to give **4** (21.6 mg), **5** (121.6 mg), **9** (68.3 mg), and **19** (26.5 mg). Fraction A4 (1.8 g) was subjected to silica gel column chromatography using petroleum ether–Me_2CO (7:3) and preparative HPLC (70% MeOH–H_2O, flow rate 12 ml/min) to give **11** (236.5 mg), 1**2** (83.4 mg), **14** (74.8 mg), and **15** (33.8 mg). The separation of fraction B (8.64 g) by silica gel column chromatography eluted with petroleum ether–Me_2CO (9:1, 8:2, 7:3, 6:4, 5:5) yielded mixtures B1–B5. Fraction B3 (1.6 g) was subjected to silica gel column chromatography using petroleum ether–Me_2CO (7:3) and preparative HPLC (70% MeOH–H_2O, flow rate 12 ml/min) to give **6** (11.6 mg), **8** (56.4 mg),

13 (64.5 mg), and **18** (92.6 mg). Fraction B4 (2.2 g) was subjected to silica gel column chromatography using petroleum ether–Me_2CO (6:4) and preparative HPLC (66% MeOH–H_2O, flow rate 12 ml/min) to give **3** (15.9 mg), **10** (28.1 mg), **16** (16.9 mg), and **17** (41.6 mg).

*3.3.1 Rubrilignan A (**1**)*

Yellow gum, $[\alpha]_D^{25.2}$ −36.5 (*c* 0.25, MeOH). CD (*c* 0.05, MeOH): $\Delta\varepsilon_{250\,nm}$ −22.6, $\Delta\varepsilon_{238\,nm}$ −15.4, $\Delta\varepsilon_{220\,nm}$ +8.22, $\Delta\varepsilon_{210\,nm}$ −2.53. UV (MeOH) λ_{max} (log ε): 212 (4.16), 252 (3.36), 318 (0.94) nm. IR (KBr) ν_{max}: 3087, 2928, 2848, 1716, 1618, 1590, 1456, 1358, 1080, 1048, 960, 852 cm^{-1}. ^1H and ^{13}C NMR spectral data see Table 1. ESI-MS: *m/z* 475 $[M + H]^+$. HR-ESI-MS: *m/z* 475.2337 $[M + H]^+$ (calcd for $C_{26}H_{35}O_8$, 475.2332).

*3.3.2 Rubrilignan B (**2**)*

Yellow gum, $[\alpha]_D^{25.0}$ −27.6 (*c* 0.25, MeOH). CD (*c* 0.05, MeOH): $\Delta\varepsilon_{250\,nm}$ −29.2, $\Delta\varepsilon_{240\,nm}$ −19.5, $\Delta\varepsilon_{220\,nm}$ +10.6, $\Delta\varepsilon_{210\,nm}$ −2.51. UV (MeOH) λ_{max} (log ε): 210 (4.26), 252 (3.38), 316 (0.88) nm. IR (KBr) ν_{max}: 3085, 2926, 2850, 1720, 1616, 1586, 1460, 1350, 1094, 1055, 958, 847 cm^{-1}. ^1H and ^{13}C NMR spectral data see Table 1. ESI-MS: *m/z* 475 $[M + H]^+$. HR-ESI-MS: *m/z* 475.2327 $[M + H]^+$ (calcd for $C_{26}H_{35}O_8$, 475.2332).

3.4 Anti-HIV-1 assay

The cytotoxicity assay against C8166 cells (CC_{50}) was assessed using the MTT method and anti-HIV-1 activity was evaluated by the inhibition assay for the cytopathic effects of HIV-1 (EC_{50}) [20].

Acknowledgements

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References

[1] Editorial Committee of the Pharmacopoeia of P.R. China, *Pharmacopoeia of the People's Republic of China (Part 1)* (Pharmacopoeia Commission of the Ministry of Public Health of PRC, Beijing, 1990), p. 454.
[2] J.B. Chang, J. Reiner, and J.X. Xie, *Chem. Rev.* **105**, 4581 (2005).
[3] W.L. Xiao, R.T. Li, S.X. Huang, J.X. Pu, and H.D. Sun, *Nat. Prod. Rep.* **25**, 871 (2008).
[4] C. Lei, W.L. Xiao, S.H. Huang, J.J. Chen, J.X. Pu, and H.D. Sun, *Tetrahedron* **66**, 2306 (2010).
[5] W.L. Xiao, Y.Q. Gong, R.R. Wang, Z.Y. Weng, X. Luo, X.N. Li, G.Y. Yang, and H.D. Sun, *J. Nat. Prod.* **72**, 1678 (2009).
[6] G.Y. Yang, W.L. Xiao, Y. Chang, R.R. Wang, J.X. Pu, X.M. Gao, C. Lei, and H.D. Sun, *Helv. Chim. Acta* **91**, 1871 (2008).
[7] W.L. Xiao, L.M. Yang, N.B. Gong, L. Wu, R.R. Wang, J.X. Pu, X.N. Li, and H.D. Sun, *Org. Lett.* **8**, 991 (2006).
[8] M. Chen, N. Kilgore, K.H. Lee, and D.F. Chen, *J. Nat. Prod.* **69**, 1697 (2006).
[9] W.L. Xiao, S.Y. Yang, L.M. Yang, G.Y. Yang, R.R. Wang, H.B. Zhang, W. Zhao, and H.D. Sun, *J. Nat. Prod.* **73**, 221 (2010).
[10] W.L. Xiao, X.L. Li, R.R. Wang, L.M. Yang, L.M. Li, S.H. Huang, J.X. Pu, and H.D. Sun, *J. Nat. Prod.* **70**, 1056 (2007).
[11] G.Y. Yang, Y.K. Li, R.R. Wang, X.N. Li, W.L. Xiao, L.M. Yang, J.X. Pu, Y.T. Zheng, and H.D. Sun, *J. Nat. Prod.* **73**, 915 (2010).
[12] G.Y. Yang, Y.K. Li, R.R. Wang, W.L. Xiao, L.M. Yang, J.X. Pu, Y.T. Zheng, and H.D. Sun, *J. Asian. Nat. Prod.* **12**, 470 (2010).
[13] D.D. Ayres and J.D. Loike, *Lignans: Chemical, Biological and Clinical Properties* (Cambridge University Press, Cambridge, 1990).
[14] Y. Ikeya, H. Kanatani, M. Hakozaki, H. Taguchi, and H. Mitsuhashi, *Chem. Pharm. Bull.* **36**, 3974 (1988).

[15] Y. Ikeya, E. Miki, M. Okada, H.J.G. Mitsuhashi, and J.G. Chai, *Chem. Pharm. Bull.* **38**, 1408 (1990).
[16] Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.* **27**, 1383 (1979).
[17] Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.* **26**, 328 (1978).
[18] C. Lei, S.X. Huang, J.J. Chen, J.X. Pu, L.B. Yang, Y. Zhao, J.P. Liu, X.M. Gao, W.L. Xiao, and H.D. Sun, *Chem. Pharm. Bull.* **55**, 1281 (2007).
[19] Y.W. Choi, S. Takamatsu, S.I. Khan, P.V. Srinivas, D. Ferreira, J.P. Zhao, and I.A. Khan, *J. Nat. Prod.* **69**, 356 (2006).
[20] J.H. Wang, S.C. Tam, H. Huang, D.Y. Ouyang, Y.Y. Wang, and Y.T. Zheng, *Biochem. Biophys. Res. Commun.* **317**, 965 (2004).