

Alstonic acids A and B, unusual 2,3-secofernane triterpenoids from *Alstonia scholaris*

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ABSTRACT

2,3-Secofernane triterpenoids, alstonic acids A (**1**) and B (**2**), were isolated from the leaves of *Alstonia scholaris* together with an indole alkaloid, *N*¹-methoxymethyl picrinine (**3**). Their structures were established from MS and NMR spectroscopic analyses and confirmed by single crystal X-ray diffraction analysis.

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1. Introduction

The genus *Alstonia* (Apocynaceae) is widely distributed throughout the tropical regions of Africa and Asia. The phytochemical constituents of *Alstonia* sp. have been extensively investigated; nearly 400 compounds have been isolated and characterized (Cai et al., 2008). Most of the compounds identified so far are indole and quinoline alkaloids (Abe et al., 1989; Atta-ur-Rahman et al., 1985, 1987; Cai et al., 2007, 2008; Macabeo et al., 2005; Salim et al., 2004; Yamauchi et al., 1990; Zhou et al., 2005). *Alstonia scholaris* (Linn.) R. Br. is a popular plant in Chinese medicine, where its leaves have been historically used in “Dai” ethnopharmacy to treat chronic respiratory diseases. The leaf extract, developed as a commercially available traditional Chinese medicine, has also been prescribed in hospitals and sold over-the-counter in drug stores (Cai et al., 2008).

As part of our effort to discover structurally diverse and biologically active secondary metabolites from local medicinal plants, the phytochemical investigation of the leaves of *A. scholaris* has led to the isolation of alstonic acids A and B (**1–2**), new 2,3-secofernane-type triterpenoids, as well as a new monoterpene indole alkaloid, *N*¹-methoxymethyl picrinine (**3**), together with six known alkaloids, picrinine (**4**) (Abe et al., 1989), 5 α -methoxystrictamine (**5**) (Zhou et al., 2005), picralinal (**6**) (Abe et al., 1989), 19,20-(*E*)-vallesamine (**7**) (Atta-ur-Rahman et al., 1987), leuconolam (**8**) (Goh et al., 1984), and scholaricine (**9**) (Atta-ur-Rahman et al., 1985). To the best of our knowledge, this report is the first to document naturally

occurring 2,3-secofermanes. The cyclization between C-3 and C-9 within alstonic acid B (**2**) is unprecedented in triterpenoids. The structural elucidation of these unique 2,3-secofermanes is described below.

2. Results and discussion

Compound **1** was isolated as colourless needles. Its molecular formula was determined to be C₃₀H₄₈O₃ on the basis of negative-ion HRESIMS at *m/z* 455.3512 (calcd. for C₃₀H₄₇O₃, 455.3525), in combination with analysis of the ¹³C NMR (DEPT) spectrum. The IR spectrum showed absorption bands at 1727, 1699 cm^{−1}, ascribable to carbonyl groups. The ¹³C NMR spectrum (Table 1) exhibited 30 carbon signals, including a carboxylic carbonyl and aldehyde carbonyl resonances at δ 174.6 (s), 207.3 (d), a tetra-substituted double bond at δ 136.2 (s), 131.3 (s), and eight up-field methyl signals from δ 14.4–23.9 ppm. The following ¹H NMR signals (Table 1) were readily distinguishable: an aldehyde singlet at δ 9.77, two AB methylene protons at δ 2.72 (d, *J* = 14.5 Hz), 2.87 (d, *J* = 14.5 Hz), a relative down-field methine proton at δ 2.90 (dd, *J* = 3.9, 3.7 Hz), six methyl singlets at δ 0.71, 0.74, 0.97, 0.99, 1.19, and 1.28, as well as two methyl doublets at δ 0.84 (d, *J* = 6.5 Hz), 0.89 (d, *J* = 6.5 Hz). The NMR spectroscopic data were similar to those of fern-8-ene (Ageta et al., 1994), except for the signals ascribed to ring A, which suggest that the compound is a *seco*-A-ring fernane triterpenoid derivative.

The following HMBC correlations (Table 1) were observed: from the above-mentioned AB methylene protons to a carboxyl carbon at δ 174.6 (s, C-2), from δ 0.97 (s, Me-23) and 1.19 (s, Me-24) to an aldehyde carbon at δ 207.3 (d, C-3), establishing that the

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Table 1NMR spectroscopic data for alstonic acids A (**1**) and B (**2**).

No.	Alstonic acid A (1) ^a			Alstonic acid B (2) ^b		
	δ_{H} (J in Hz)	δ_{C} mult.	HMBC ^c	δ_{H} (J in Hz)	δ_{C} mult.	HMBC ^c
1	2.72 d (14.5) 2.87 d (14.5)	46.4 t	2, 5, 9, 25	2.25 d (15.4) 3.02 d (15.4)	38.5 t	2, 5, 9, 25
2		174.6 s			178.3 s	
3	9.77 s	207.3 d	5, 24		222.5 s	
4		49.5 s			46.8 s	
5	2.90 dd (3.9, 3.7)	42.3 d	1, 3, 9, 24	2.25 br s	45.6 d	3, 7
6	1.86 m, H _{β} 2.28 m, H _{α}	20.1 t	4, 8, 10	2.19 br dd (19.1, 3.1), H _{β} 2.55 br d (19.1), H _{α}	28.3 t	4, 8, 10
7	2.00, 2.05 m	23.4 t		5.58 br d (3.1)	121.0 d	5, 9, 14
8		136.2 s			143.8 s	
9		131.3 s			58.1 s	
10		41.3 s			42.7 s	
11	1.91 m, H _{β} 2.06 m, H _{α}	20.9 t		1.36 m, H _{α} 1.76 m, H _{β}	19.0 t	3, 8, 10, 13
12	1.28, 1.39 m	31.1 t		1.25, 1.65 m	29.8 t	9, 14, 27
13		37.1 s			36.9 s	
14		41.3 s			44.0 s	
15	1.25 m, H _{α} 1.75 m, H _{β}	28.3 t		1.30 m, H _{α} 1.69 m, H _{β}	29.9 t	
16	1.43 m, H _{β} 1.64 m, H _{α}	36.1 t	18, 21, 28	1.53 m, H _{β} 1.70 m, H _{α}	35.5 t	
17		43.0 s			42.9 s	
18	1.45 m	52.9 d		1.53 m	52.0 d	
19	1.37 m, H _{α} 1.47 m, H _{β}	20.7 t		1.20 m, H _{α} 1.39 m, H _{β}	20.0 t	
20	1.15 m, H _{α} 1.75 m, H _{β}	28.6 t		1.19 m, H _{α} 1.84 m, H _{β}	28.3 t	
21	0.88 m	59.7 d	16, 28	0.98 m	59.6 d	
22	1.43 m	31.0 d		1.44 m	30.7 d	
23	0.97 s	23.9 q	3, 5, 24	1.19 s ^d	28.8 q ^e	3, 5, 24
24	1.19 s	19.8 q	3, 5, 23	1.20 s ^d	29.0 q ^e	3, 5, 23
25	1.28 s	23.2 q	1, 5, 9	1.00 s	22.8 q ^f	1, 5, 9
26	0.99 s	21.4 q	8, 13, 15	0.96 s	20.9 q	8, 13, 15
27	0.71 s	16.6 q	12, 14, 18	0.71 s	15.6 q	12, 14, 18
28	0.74 s	14.4 q	16, 18, 21	0.76 s	14.9 q	16, 18, 21
29	0.89 d (6.5)	22.3 q	21, 30	0.88 d (6.6)	22.0 q	21, 30
30	0.84 d (6.5)	23.2 q	21, 29	0.82 d (6.6)	22.9 q ^f	21, 29

^{a,b}Determined for C₅D₅N (δ_{H} 8.71 ppm, δ_{C} 149.9 ppm as int. standard) and CDCl₃ (δ_{H} 7.26 ppm, δ_{C} 77.0 ppm), respectively.^cOnly important and discernable correlations were listed.^{d,e,f}Interchangeable.

carboxyl and aldehyde groups were positioned at C-2 and C-3, respectively. Therefore, the triterpene acid was elucidated as 2,3-*seco*-3-oxoferan-8-en-2-oic acid, and named alstonic acid A. The structure of **1** was finally confirmed by single crystal X-ray diffraction, and a perspective ORTEP diagram of the molecule is shown in Fig. 2. Although 3,4-*seco*-A-ring triterpenoids have sometimes been isolated from natural sources, only a few cases of 2,3-*seco* derivatives have been reported up to now (Baas, 1985; Toriumi et al., 2003).

Compound **2**, colourless needles, possesses a molecular formula of C₃₀H₄₆O₃ based on the negative-ion HRESIMS at m/z 453.3359 (calcd. for C₃₀H₄₅O₃, 453.3368) and supported by analysis of the ¹³C NMR (DEPT) spectrum. The IR spectrum showed the absorption bands of carbonyl (1737, 1702 cm⁻¹) and double bond (3039, 1635 cm⁻¹) groups. The NMR spectroscopic characters (Table 1) were similar to those of alstonic acid A (**1**), suggesting that **2** was also a 2,3-*seco*feran triterpene acid derivative. However, there were some prominent differences as follows: the resonances of the aldehyde and the tetra-substituted double bond were absent and replaced by those of a newly arisen ketone at δ_{C} 222.5 (s, C-3) and a tri-substituted olefin at δ_{H} 5.58 (1H, br d, J = 3.1 Hz), δ_{C} 121.0 (d, C-7), 143.8 (s, C-8), respectively, in the NMR spectrum of **2**. Considering eight degrees of unsaturation, including the contribution of five rings, the C-3 ketone group must connect with a certain carbon atom of the triterpenoid scaffolding to generate a new ring, and the linked position was determined as C-9 based

on the following important HMBC correlations (Table 1): from δ_{H} 1.36, 1.76 (each m, H-11) to δ_{C} 222.5 (s, C-3), from δ_{H} 2.25, 3.02 (each d, J = 15.4 Hz, H-1), 5.58 (br d, J = 3.1 Hz, H-7) and 1.00 (s, Me-25) to δ_{C} 58.1 (s, C-9).

The configuration of H-5 was unambiguously determined to be in an α orientation (i.e., equatorial bond) based on the following evidence: (1) the proton H-5 showed a broad singlet in ¹H NMR spectrum (if axial, it should exhibit a typical double doublet, J $\approx$ 11.0, 4.0 Hz); and (2) the ROESY correlation (Fig. 3) between H-5 and H-6 α was observed. Accordingly, the cyclization between C-3 and C-9 must span above the ring-B, so the relative configuration of C-9 was deduced to β . Consequently, the structure of **2** was established as shown in Fig. 1 and named alstonic acid B. The biosynthetic pathway (Fig. 4) of **2** involves an unprecedented C–C cyclization between C-3 and C-9.

Compound **3**, obtained as colourless, crystalline powder, has a molecular formula of C₂₂H₂₆N₂O₄ based on the positive-ion HRESIMS, showing a quasi-molecular ion peak at m/z 383.1965 (calcd. for C₂₂H₂₇N₂O₄, 383.1970), and the ¹³C NMR (DEPT) spectrum. The UV spectrum showed absorptions at 238, 287 nm, typical of a modified indoline chromophore. The NMR spectrum of **3** was very similar to that of picrinine (**4**) (Abe et al., 1989), also isolated from this species. Nevertheless, there were several additional observed signals in **3**: a down-field methylene resonance at δ_{H} 4.74, 4.95 (each 1H, d, J = 11.0 Hz), δ_{C} 76.7 (t) and a methoxyl group at δ_{H} 3.40 (3H, s), δ_{C} 55.5 (q). Significant HMBC correlations (Table 2) from δ_{H} 4.74,

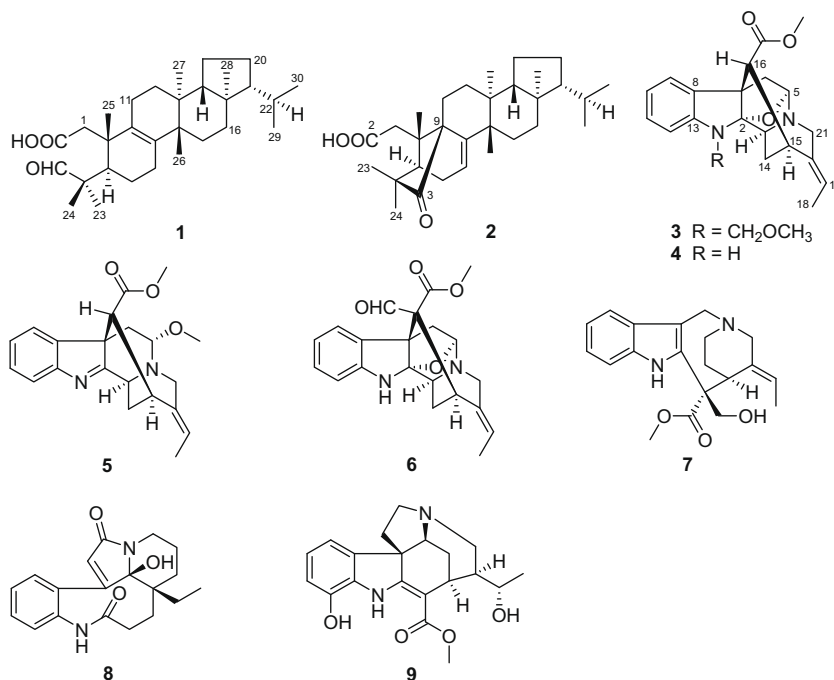


Fig. 1. Structures of 1–9 isolated from *A. scholaris*.

4.95 (each 1H, d, $J = 11.0$ Hz) to δ_{C} 106.8 (s, C-2), 147.8 (s, C-13) and 55.5 (q), and from δ_{H} 3.40 (3H, s) to δ_{C} 76.7 (t), were observed, indicating that a methoxymethyl group must attach to the nitrogen atom in the indoline ring. Thus, the structure of **3** was determined as *N*¹-methoxymethyl picrinine.

It should be mentioned that the configuration of 5-OCH₃ in **5** was wrongly assigned in the original literature (Zhou et al., 2005)

and should be revised to be in an α orientation. This discrepancy was observed by comparing the NMR spectroscopic data, especially the characteristic coupling constants, with those of analogues (Abe et al., 1994, 1998). The adjustment was also supported by the observed ROESY correlations: H-5 β $\leftrightarrow$ H-6 β , H-5 β $\leftrightarrow$ H-21 β , and H-14 α $\leftrightarrow$ H-21 α .

3. Concluding remarks

Compounds **1** and **2** have been reported as the first known examples of 2,3-secofernanane triterpenoids. Their presence as markers may be helpful in chemotaxonomical classifications. Biological investigations for these compounds are underway.

4. Experimental

4.1. General experimental procedures

Melting points were measured on a PHMK 79/2289 micro-melting point apparatus and were presented as uncorrected. Optical rotations were measured on a Horiba SEPA-300 polarimeter. UV spectra were recorded on a Shimadzu UV-2401PC spectrophotometer. IR spectra were obtained using a Bruker Tensor 27 FT-IR spectrometer with KBr pellets. NMR spectra were acquired at room temperature with Bruker DRX-500 and AV-400 instruments. ESIMS and HRESIMS data were obtained with an API QSTAR Pulsar i spectrometer. X-ray crystallographic data were collected on a Bruker Smart APEX II CCD diffractometer with graphite-monochromated Mo K α radiation. Silica gel (200–300 mesh, Qingdao Marine Chemical Inc., China) and Sephadex LH-20 (Amersham Biosciences, Sweden) were used for column chromatography. Fractions were monitored by silica gel plates immersed in vanillin-H₂SO₄ in ethanol or Dragendorff's reagent, in combination with Agilent 1200 reversed-phase HPLC (Eclipse XDB-C18 column, 5 μm , 4.6 $\times$ 150 mm, 50–100% MeOH in H₂O over 8 min followed by 100% MeOH to 15 min, 1 ml/min, 25 $^{\circ}\text{C}$).

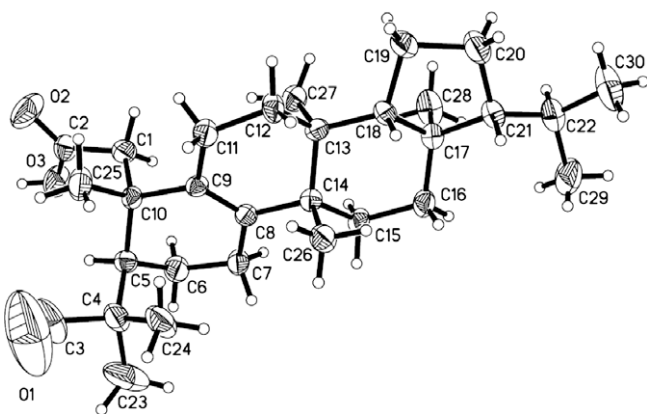


Fig. 2. Molecular structure of **1** generate by X-ray analysis.

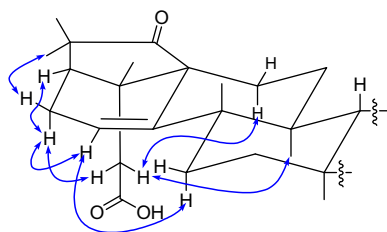


Fig. 3. Key ROESY correlation of **2**.

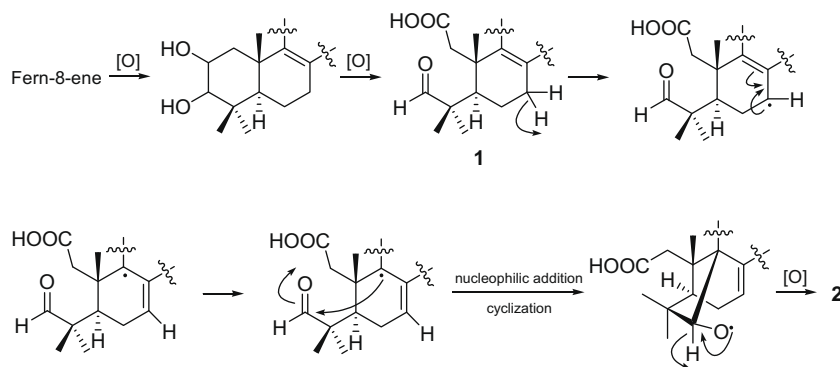


Fig. 4. The proposed biosynthetic pathway of alstonic acid (**2**).

Table 2

NMR spectroscopic data for *N*¹-methoxymethyl picrinine (**3**) and 5 α -methoxystrictamine (**5**).

No.	<i>N</i> ¹ -Methoxymethyl picrinine (3)			5 α -Methoxystrictamine (5)
	δ_H (J in Hz)	δ_C mult.	HMBC	δ_H (J in Hz)
2		106.8 s		
3	3.82 d (4.6)	50.5 d	7, 15, 21	4.48 d (5.1)
5	4.85 d (2.0)	87.2 d	2, 3, 7	3.87 d (4.0), H $_{\beta}$
6	2.26 dd (13.6, 2.0) 3.43 d (13.6)	39.9 t	2, 8, 16	2.20 d (15.0), H $_{\beta}$ 3.72 dd (15.0, 4.0), H $_{\alpha}$
7		51.0 s		
8		134.4 s		
9	7.13 d (7.3)	124.7 d	7, 11, 13	7.61 d (7.7)
10	6.82 dd (7.9, 7.3)	121.0 d	8, 12	7.31 dd (7.7, 7.3)
11	7.15 dd (7.9, 7.9)	128.2 d	9, 13	7.12 dd (7.3, 7.3)
12	6.85 d (7.9)	109.0 d	8, 10	7.38 d (7.3)
13		147.8 s		
14	1.85 dd (14.3, 2.6) 2.18 ddd (14.3, 4.6, 3.5)	25.7 t	2, 16, 20	1.75 dd (14.0, 3.0), H $_{\beta}$ 2.67 ddd (14.0, 5.1, 2.1), H $_{\alpha}$
15	3.30 br s	31.0 d	19, 21	3.43 br s
16	2.44 d (3.4)	51.9 d	2, 6, 8, 14, 20	1.90 d (3.8)
18	1.49 dd (6.9, 2.0)	12.7 q	20	1.53 dd (6.8, 1.7)
19	5.43 br q (6.9)	121.0 d	15, 21	5.49 br q (6.8)
20		135.0 s		
21	3.13 d (17.7) 3.79 br d (17.7)	46.2 t	3, 5, 15, 19	3.07 d (17.1), H $_{\beta}$ 4.05 br d (17.1), H $_{\alpha}$
COOCH ₃		172.2 s		
COOCH ₃	3.65 s	51.5 q	COOCH ₃	3.69 s
NCH ₂ O	4.74 d (11.0) 4.95 d (11.0)	76.7 t	2, 13, OCH ₃	
CH ₂ OCH ₃	3.40 s	55.5 q	NCH ₂ O	
5-OCH ₃				3.21 s

Determined in CDCl₃ (δ_H 7.26 ppm, δ_C 77.0 ppm as int. standard).

4.2. Plant material

Leaves of *A. scholaris* were collected in Yunnan Province, China and identified by Prof. Dr. Hua Peng, Kunming Institute of Botany, CAS. A voucher specimen (BBP2008003AS) was deposited in the Herbarium of Kunming Institute of Botany.

4.3. Extraction and isolation

Air-dried, powdered leaves (8.5 kg) of *A. scholaris* were soaked with EtOH:H₂O (25 L $\times$ 3, 95:5, v/v, with each soaking for 3 days) at room temperature and filtered. The filtrate was concentrated *in vacuo* to give a residue (~500 g), which was subjected to silica gel column chromatography (CC) with a gradient elution system of petroleum ether–acetone (100:0 $\rightarrow$ 0:100) to obtain 18 fractions. Fraction-4 (3.0 g) mainly contained the triterpene acids, eluted with petroleum ether–acetone (90:10), was repeatedly separated and purified by silica gel (petroleum ether:EtOAc = 20:1) and Sephadex LH-20 CC and recrystallization to afford compounds

1 (164 mg) and **2** (13 mg). Fraction-17 (20 g) eluted with acetone was further separated and purified by silica gel (CHCl₃:MeOH = 100:1) and Sephadex LH-20 (CHCl₃:MeOH = 1:1) CC, as well as by recrystallization to yield alkaloid **3** (46 mg).

4.4. Alstonic acid A (**1**)

Colourless needles (CHCl₃/MeOH); m.p. 244–246 °C; R_f = 0.40 (petroleum ether:EtOAc = 1:1); $[\alpha]_D^{22}$ –4.4 (c 0.23, CHCl₃:MeOH = 1:1); IR (KBr) ν_{max} cm^{–1}: 2928, 2870, 2686, 1727, 1699, 1468, 1406, 1382, 1310, 1241; for ¹H and ¹³C NMR spectroscopic data, see Table 1; ESIMS (neg.) m/z : 455 [M – H][–]; HRESIMS (neg.) m/z : 455.3512 (calcd. for C₃₀H₄₇O₃, 455.3525).

4.5. Alstonic acid B (**2**)

Colourless needles (CHCl₃); m.p. 282–284 °C; R_f = 0.60 (petroleum ether:EtOAc = 1:1); $[\alpha]_D^{23}$ +191.4 (c 0.43, CHCl₃); IR (KBr) ν_{max} cm^{–1}: 3039, 2939, 2869, 1737, 1702, 1635, 1468, 1408, 1380, 1312,

1233; for ^1H and ^{13}C NMR spectroscopic data, see Table 1; ESIMS (neg.) m/z : 453 $[\text{M} - \text{H}]^-$; HRESIMS (neg.) m/z : 453.3359 (calcd. for $\text{C}_{30}\text{H}_{45}\text{O}_3$, 453.3368).

4.6. N^1 -Methoxymethyl picrinine (**3**)

Colourless, crystalline powder (CHCl_3); m.p. 181–183 °C; $R_f = 0.50$ (CHCl_3 :MeOH = 20:1), $t_R = 8.35$ min; $[\alpha]_D^{27} -56.7$ (c 0.15, CHCl_3); UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 238 (3.76), 287 (3.26); IR (KBr) ν_{max} cm^{-1} : 3018, 1737, 1609, 1481, 1190, 1172, 1116, 1077; for ^1H and ^{13}C NMR spectroscopic data, see Table 2; ESIMS (pos.) m/z : 405 $[\text{M} + \text{Na}]^+$, 383 $[\text{M} + \text{H}]^+$, 351 $[\text{M} - \text{OCH}_3]^+$; HRESIMS (pos.) m/z : 383.1965 (calcd. for $\text{C}_{22}\text{H}_{27}\text{N}_2\text{O}_4$, 383.1970).

4.7. X-ray crystallographic analysis of alstonic acid A (**1**)

$\text{C}_{30}\text{H}_{48}\text{O}_3$, MW = 456.68, monoclinic, space group C2, with $a = 29.289(7)$ Å, $b = 7.6106(19)$ Å, $c = 12.004(3)$ Å, $\beta = 94.914(3)^\circ$, $V = 2666.0(11)$ Å³, $Z = 4$, $D_{\text{calcd}} = 1.138$ g/cm³, $\lambda = 0.71073$ Å, $\mu(\text{Mo K}\alpha) = 0.071$ mm⁻¹, and $F(000) = 1008$, and $T = 298(2)$ K. A colourless crystal of dimensions $0.21 \times 0.13 \times 0.04$ mm was selected for X-ray analysis. A total of 11673 reflections, collected in the range $1.40^\circ \leq \theta \leq 28.31^\circ$, yielded 6024 unique reflections. The structure was solved using direct methods and was refined by full-matrix least-squares on F^2 values for 2268 $I > 2\sigma(I)$. Hydrogen atoms were fixed at calculated positions. The final indices were $R_1 = 0.0820$, $wR_2 = 0.1779$ and had a goodness-of-fit = 0.948.

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Appendix A. Supplementary data

Crystallographic data for structure **1** is deposited at the Cambridge Crystallographic Data Centre as supplementary publication

no. CCDC 705372. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.phytochem.2009.03.007.

References

- Abe, F., Chen, R.F., Yamauchi, T., Marubayashi, N., Ueda, I., 1989. Alschomine and isoalschomine, new alkaloids from the leaves of *Alstonia scholaris*. Chem. Pharm. Bull. 37, 887–890.
- Abe, F., Yamauchi, T., Padolina, W.G., 1994. Indole alkaloids from leaves of *Alstonia macrophylla* in the Philippines. Phytochemistry 35, 253–257.
- Abe, F., Yamauchi, T., Shibuya, H., Kitagawa, I., Yamashita, M., 1998. Indole alkaloids from the leaves of *Alstonia villosa* in Sunbawa (*Alstonia* 6). Chem. Pharm. Bull. 46, 1235–1238.
- Ageta, H., Shiojima, K., Arai, Y., Suzuki, H., Kiyotani, T., 1994. NMR spectra of triterpenoids. II. Hopenes and migrated hopenes. Chem. Pharm. Bull. 42, 39–44.
- Atta-ur-Rahman, F.R.S., Alvi, K.A., Abbas, S.A., Voelter, W., 1987. Isolation of 19,20-Z-vallesamine and 19,20-E-vallesamine from *Alstonia scholaris*. Heterocycles 26, 413–419.
- Atta-ur-Rahman, F.R.S., Asif, M., Ghazala, M., Fatima, J., Alvi, K.A., 1985. Scholaricine, an alkaloid from *Alstonia scholaris*. Phytochemistry 24, 2771–2773.
- Baas, W.J., 1985. Naturally occurring seco-ring-A-triterpenoids and their possible biological significance. Phytochemistry 24, 1875–1889.
- Cai, X.H., Du, Z.Z., Luo, X.D., 2007. Unique monoterpenoid indole alkaloids from *Alstonia scholaris*. Org. Lett. 9, 1817–1820.
- Cai, X.H., Tan, Q.G., Liu, Y.P., Feng, T., Du, Z.Z., Li, W.Q., Luo, X.D., 2008. A cage-monoterpene indole alkaloid from *Alstonia scholaris*. Org. Lett. 10, 577–580.
- Goh, S.H., Wei, C., Ali, A.R.M., 1984. Strychnos-aspidosperma alkaloids and a novel hydroxydilatam artefact from *Leuconotis griffithii* (Apocynaceae). Tetrahedron Lett. 25, 3483–3484.
- Macabeo, A.P.G., Krohn, K., Gehle, D., Read, R.W., Brophy, J.J., Cordell, G.A., Franzblau, S.G., Aguinaldo, A.M., 2005. Indole alkaloids from the leaves of Philippine *Alstonia scholaris*. Phytochemistry 66, 1158–1162.
- Salim, A.A., Garson, M.J., Craik, D.J., 2004. New indole alkaloids from the bark of *Alstonia scholaris*. J. Nat. Prod. 67, 1591–1594.
- Toriumi, Y., Kakuda, R., Kikuchi, M., Yaoita, Y., Kikuchi, M., 2003. New triterpenoids from *Gentiana lutea*. Chem. Pharm. Bull. 51, 89–91.
- Yamauchi, T., Abe, F., Chen, R.F., Nonaka, G.I., Santisuk, T., Padolina, W.G., 1990. Alkaloids from the leaves of *Alstonia scholaris* in Taiwan, Thailand, Indonesia and the Philippines. Phytochemistry 29, 3547–3552.
- Zhou, H., He, H.P., Luo, X.D., Wang, Y.H., Yang, X.W., Di, Y.T., Hao, X.J., 2005. Three new indole alkaloids from the leaves of *Alstonia scholaris*. Helv. Chim. Acta 88, 2508–2512.