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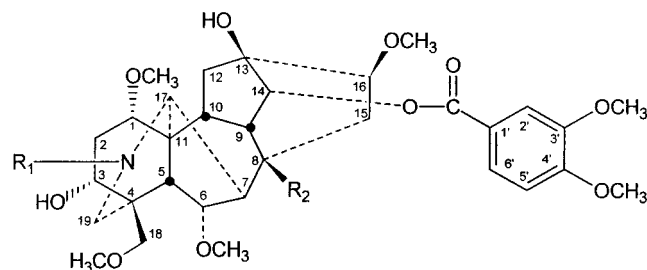
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The roots of *Aconitum falconeri* have yielded two new norditerpenoid alkaloids, faleoconitine (**1**) and 3'-methoxyacoforestinine (**2**) along with the known compounds, karakoline, 3-hydroxy-2-methyl-4H-pyran-4-one, and 3,4-dimethoxymethylbenzoate, which have been isolated for the first time from this plant. The previously reported pseudoaconitine (**3**) was also isolated. Compounds **1** and **3** were found to be moderate inhibitors of the enzyme acetylcholinesterase.

*Aconitum* species (Ranunculaceae) produce diterpenoid and norditerpenoid alkaloids that are generally of the aconitine and lycoctonine types.<sup>1</sup> *Aconitum falconeri* Stapf. is found widely in the Azad Kashmir, Baluchistan, and Chitral regions of Pakistan<sup>2</sup> and the Himalayan and Garhwal regions of India.<sup>3</sup> It is widely used in indigenous systems of medicine for its cardiotonic and sedative properties.<sup>4</sup> The roots of *Aconitum* plants are frequently employed for the treatment of rheumatism and neuralgia.<sup>5</sup> Previous work on these plants has resulted in the isolation of a large number of alkaloids.<sup>6–9</sup> During our work on diterpenoid alkaloid-bearing plants, we have isolated two new alkaloids (**1** and **2**) and four known compounds, karakoline, 3-hydroxy-2-methyl-4H-pyran-4-one, 3,4-dimethoxymethylbenzoate, and pseudoaconitine (**3**) from the roots of *A. falconeri*. Alkaloids **1** and **3** have shown moderate inhibitory activity against the enzyme acetylcholinesterase.



- 1 R<sub>1</sub> = CHO, R<sub>2</sub> = OCOCH<sub>3</sub>  
 2 R<sub>1</sub> = CH<sub>2</sub>CH<sub>3</sub>, R<sub>2</sub> = OCH<sub>2</sub>CH<sub>3</sub>  
 3 R<sub>1</sub> = CH<sub>2</sub>CH<sub>3</sub>, R<sub>2</sub> = OCOCH<sub>3</sub>

### Results and Discussion

Compound **1** was isolated by column and preparative TLC and finally crystallized from MeOH. The HREIMS of **1** showed the molecular ion at  $m/z$  689.3042 corresponding to the molecular formula C<sub>35</sub>H<sub>47</sub>NO<sub>13</sub> (calcd 689.3047). The IR spectrum of **1** (KBr) showed the presence of hydroxyl (3515 cm<sup>-1</sup>), carbonyl (1717, 1722 cm<sup>-1</sup>), and aromatic C=C (1601 cm<sup>-1</sup>) groups. The <sup>1</sup>H NMR spectrum of **1** closely resembled that of pseudoaconitine (**3**),<sup>8</sup> showing four 3H singlets at  $\delta$  3.50, 3.13, 3.22, and 3.27, which were assigned to the four aliphatic methoxy groups. Two additional sets of downfield 3H singlets at  $\delta$  3.88 and 3.91 were assigned to the aromatic methoxy groups. A signal at  $\delta$  1.78 (3H, s) was due to protons of an acetoxy-methyl substituent at

C-8. A <sup>1</sup>H doublet at  $\delta$  4.84 ( $J_{14,9}$  = 4.8 Hz, H-14 $\beta$ ) was assigned to C-14H and indicated the presence of a geminal -OH group at C-13. The <sup>13</sup>C NMR spectrum of **1** showed 34 carbon signals, with the signal for the *N*-formyl carbon not being clearly visible in the spectrum recorded at room temperature due to atropisomerism. The structure of faleoconitine (**1**) was, therefore, confirmed by X-ray diffraction. A suitable crystal formed in the monoclinic space group *P*2<sub>1</sub> was selected for the study. Accurate lattice constants were  $a$  = 11.945(2),  $b$  = 12.703(3), and  $c$  = 12.011(4) Å;  $\beta$  = 100.62(2). Two molecules of the composition C<sub>35</sub>H<sub>47</sub>NO<sub>13</sub> formed the asymmetric unit. All unique diffraction maxima with  $2\theta \leq 135$  were collected using  $\theta - 2\theta$  scans. Altogether, 3399 unique reflections were collected, and 2970 (87.37%) were judged observed [ $I > 2\sigma(I)$ ] and used in calculations. The structure was solved by using direct methods and refined by full-matrix least-squares on  $F^2$  to a final discrepancy index of 0.048 ( $R_w$  = 0.1368) for observed data. A computer-generated perspective drawing of the final X-ray model is given in Figure 1. The crystal structure confirmed the presence of an *N*-formyl functionality in **1**, which is rare in the C<sub>19</sub>-diterpenoid class of alkaloids. The *N*-formyl group in the X-ray model of **1** indicated a large disorder, further confirming the existence of atropisomerism. Compound **1** was assigned the trivial name faleoconitine.

Another new alkaloid (**2**) was obtained as an amorphous solid by repeated column chromatography and finally by preparative TLC. The HREIMS of **2** showed the  $M^+$  at  $m/z$  675.3612, corresponding to the molecular formula C<sub>36</sub>H<sub>53</sub>NO<sub>11</sub> (calcd 675.3618). The IR spectrum showed the presence of hydroxyl (3610–3795 cm<sup>-1</sup>), ester carbonyl (1725, 1733 cm<sup>-1</sup>), and aromatic C=C (1601 cm<sup>-1</sup>) groups. The UV absorption at 260 nm was consistent with the presence of a benzoyl chromophore in the molecule. The <sup>1</sup>H NMR spectrum indicated the presence of a trisubstituted aromatic moiety ( $\delta$  7.70, 7.62, and 6.87). A 3H triplet at  $\delta$  1.13 ( $J_{21,22}$  = 7.10 Hz) was coupled in the COSY-45° spectrum with the diastereotopic methylene protons at  $\delta$  2.55 and 2.60, indicating the presence of an *N*-ethyl group. There were four 3H singlets at  $\delta$  3.24, 3.25, 3.29, and 3.53, which could be assigned to the four aliphatic methoxy groups. Two relatively more downfield 3H singlets at  $\delta$  3.91 and 3.92 were assigned to the aromatic methoxy methyl groups. The C-14 methine signal resonated at  $\delta$  4.81 (1H, d,  $J_{14,9}$  = 5.0 Hz, H-14 $\beta$ ) indicated the presence of a geminal  $\beta$ -OH group at C-13. The <sup>1</sup>H multiplets at  $\delta$  3.49 and 3.20 were assigned to the CH<sub>2</sub> protons of the *O*-ethyl moiety substituted at C-8. The <sup>1</sup>H NMR spectrum of **2**

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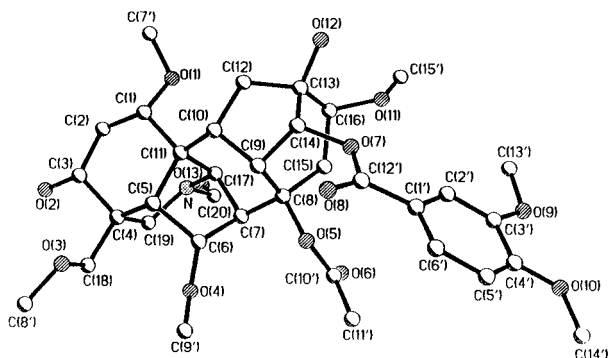


Figure 1. ORTEP diagram of X-ray crystals structure of compound 1.

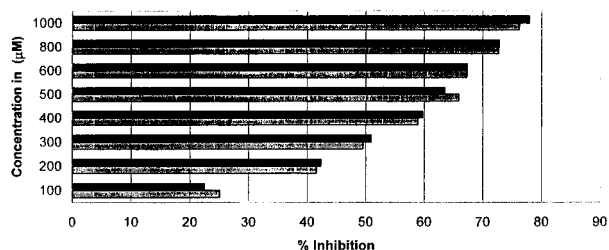


Figure 2. Inhibitory effect of various concentrations of faleoconitine (1) (gray bar) and pseudoconitine (3) (black bar) on acetylcholinesterase activity.

closely resembled that of acoforestinine,<sup>10</sup> except for the presence of an additional OCH<sub>3</sub> group at C-3' on the phenyl ring. The <sup>13</sup>C NMR spectrum of **2** showed 36 carbon signals, including 13 methine, seven methylene, two C-methyl, six O-methyl, and eight quaternary carbons. The <sup>13</sup>C NMR spectra of **2** also indicated that two of the six methoxyl groups were substituted at aromatic carbons resonating at  $\delta$  148.5 (C-3') and 152.8 (C-4'). These assignments were further confirmed with the help of HMBC interactions, which showed correlations of H-17 ( $\delta$  2.70) with C-1 ( $\delta$  83.0), C-5 ( $\delta$  48.8), and C-11 ( $\delta$  50.8), while H-5 ( $\delta$  2.36) showed interactions with C-11 ( $\delta$  50.8), C-6 ( $\delta$  82.4), and C-10 ( $\delta$  41.3). The aromatic H-6' ( $\delta$  7.70) signal showed HMBC couplings with C-4' ( $\delta$  152.8) and C-2' ( $\delta$  112.3), while H-2' ( $\delta$  7.62) was found to be coupled with the ester C=O ( $\delta$  166.1), C-4' ( $\delta$  152.8), and C-6' ( $\delta$  123.7). Similarly, H-5' ( $\delta$  6.87) was coupled with C-3' ( $\delta$  148.5) and C-1' ( $\delta$  123.3). These spectroscopic observations led to the structure **2** for this new alkaloid, which has been named 3'-methoxyacoforestinine.

The known compounds karakoline (earlier reported from *A. carmicheali*<sup>11</sup> and a number of other plants<sup>12–15</sup>), 3-hydroxy-2-methyl-4H-pyran-4-one (earlier isolated from *Larix decidua*<sup>16,17</sup>), and 3,4-dimethoxymethylbenzoate (previously isolated from *Verbascum thapsus*<sup>18</sup>) were also isolated and identified by data comparison with reported spectral data.

Faleoconitine (**1**) and pseudoconitine (**3**) have been found to be moderate inhibitors of the enzyme acetylcholinesterase. Pseudoconitine (**3**) showed a slightly greater inhibitory activity against the enzyme as compared to faleoconitine (**1**), while compound **2** was found to be inactive as an inhibitor of this enzyme. The IC<sub>50</sub> ( $\mu$ M) values of the active compounds faleoconitine (**1**) and pseudoconitine (**3**) are  $293 \pm 3.8$  and  $278 \pm 3.6$ , respectively. The effect of various concentrations of the active compounds is shown in Figure 2. Acetylcholinesterase inhibitors are potential candidates for the treatment of Alzheimer's disease.<sup>19</sup>

## Experimental Section

**General Experimental Procedures.** Melting points were determined on a Büchi 535 melting point apparatus and are

uncorrected. Optical rotations were measured on a JASCO DIP-360 polarimeter. The UV spectra were recorded in MeOH on a Shimadzu UV 240 instrument. The IR spectra were recorded on JASCO IRA-1 IR spectrophotometer. The <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> on a Bruker AM 400 NMR spectrometer at 400 MHz, while the <sup>13</sup>C NMR data were recorded on the same instrument at 100 MHz. Mass spectra were measured on JEOL HX-110 mass spectrometer.

**Plant Material.** The roots of *A. falconeri* Stapf. were purchased from a local herbal market in May 1997, at Karachi, Pakistan. The plant material was identified by Mr. Tahir Ali, plant taxonomist, Department of Botany, University of Karachi. A voucher specimen was deposited in the herbarium (KUH # 46628) of the University of Karachi.

**Extraction and Isolation.** The air-dried and powdered roots (20 kg) were soaked in 80% ethanol (50 L) at room temperature for 5 days. The EtOH extract was evaporated under a vacuum to afford a dark viscous residue. This residue was dissolved in water and defatted with *n*-hexane. The defatted aqueous extract was then extracted with chloroform at two pH levels, 2–3 (fraction A) and 9–10 (fraction B), which were adjusted by the addition of NH<sub>4</sub>OH and dilute acetic acid, respectively. The remaining aqueous layer was finally extracted with *n*-BuOH (fraction C).

Fraction A (CHCl<sub>3</sub> extract obtained from aqueous layer at pH 2–3) (14 g) was subjected to column chromatography on Si gel (500 g). The column was eluted with *n*-hexane/CHCl<sub>3</sub> mixtures and then with CHCl<sub>3</sub>/CH<sub>3</sub>OH mixtures to obtain various subfractions. The subfraction (0.95 g) obtained on elution with CHCl<sub>3</sub>/CH<sub>3</sub>OH (80:20) was found to contain two compounds. It was further purified by TLC using the solvent system CHCl<sub>3</sub>/CH<sub>3</sub>OH/diethylamine (80:20:0.5), which afforded compound **2**. Another subfraction (3.75 g) from the same column was again chromatographed on a Si gel column (125 g) and eluted with *n*-hexane/CHCl<sub>3</sub> mixtures of increasing polarities to obtain 3-hydroxy-2-methyl-4H-pyran-4-one (47.52 mg) and pseudoconitine (**3**) (95.73 mg).

Fraction B (extracted from aqueous extract at pH 9–10) was dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo to obtain the crude gum (37.37 g). This was chromatographed on a Si gel column and eluted with CHCl<sub>3</sub>/CH<sub>3</sub>OH mixture of increasing polarities, to obtain karakoline (105.7 mg) and 3,4-dimethoxymethylbenzoate (25.51 mg).

The *n*-BuOH extract (fraction C) (47.0 g) was subjected to column chromatography on Si gel and eluted first with CHCl<sub>3</sub> and then with CHCl<sub>3</sub>/CH<sub>3</sub>OH mixtures. A fraction (0.10 g) obtained on elution with CHCl<sub>3</sub>/CH<sub>3</sub>OH (70:30) afforded faleoconitine (**1**).

**Faleoconitine (1):** crystallized from MeOH as colorless crystals (21.4 mg); mp 205 °C,  $[\alpha]_D^{25} - 28^\circ$  (*c* 0.14, MeOH); UV (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 292 (2.75), 263 (3.01), 220 (3.29) nm; IR (KBr)  $\nu_{\max}$  3515, 2980, 1722, 1717, 1601 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.67 (1H, d,  $J_{6,5'} = 8.2$  Hz, H-6'), 7.58 (1H, s, H-2'), 6.88 (1H, d,  $J_{6,5'} = 8.2$  Hz, H-5'), 4.84 (1H, d,  $J_{14\beta,9} = 4.8$  Hz, H-14 $\beta$ ), 3.91, 3.88, 3.50, 3.27, 3.22, 3.13 (each 3H, s, 6  $\times$  OCH<sub>3</sub>), 1.78 (3H, s, COCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 °C)  $\delta$  170.8 (OCOCH<sub>3</sub>), 168.8 (OCOAr), 164.8 (NCHO), 152.7 (C-4'), 148.2 (C-3'), 123.1 (C-1'), 122.1 (C-6'), 111.8 (C-5'), 111.0 (C-2'), 84.8 (C-1), 83.0 (C-6), 85.7 (C-8), 78.3 (C-16), 74.8 (C-14), 77.7 (C-18), 71.5 (C-3), 74.1 (C-13), 61.1 (C-17), 58.9, 58.1, 57.8, 55.7, 55.4, 55.3 (OCH<sub>3</sub>), 49.4 (C-11), 49.0 (C-5, -19), 48.5 (C-7), 45.9 (C-9), 45.0 (C-4), 43.2 (C-10), 36.8 (C-15), 35.2 (C-2), 33.5 (C-12), 21.2 (OCOCH<sub>3</sub>); EIMS *m/z* 689 [M]<sup>+</sup> (4), 658 [M<sup>+</sup> - OCH<sub>3</sub>] (6), 629 [M<sup>+</sup> - OCH<sub>3</sub> - CHO] (77), 598 (96), 448 (38), 268 (87), 165 (100); HREIMS *m/z* 689.3042 (calcd for C<sub>35</sub>H<sub>47</sub>NO<sub>13</sub>, 689.3047).

**Crystal Data and X-ray Crystal Structure Determination of Faleoconitine (1).** Crystals of **1** suitable for X-ray diffraction analysis were obtained by recrystallization from MeOH. C<sub>35</sub>H<sub>47</sub>NO<sub>13</sub>; *M*<sub>r</sub> = 689.3047, monoclinic *a* = 11.945(2) Å, *b* = 12.703(3) Å, *c* = 12.011(4) Å,  $\beta$  = 100.62(2)°, *V* = 1791.3(8) Å<sup>3</sup>, space group *P*2<sub>1</sub> (no.4), *Z* = 2, *D*<sub>calc</sub> = 1.220 g/cm<sup>3</sup>,  $\mu$  (Cu K $\alpha$ ) = 0.714 mm<sup>-1</sup>, *F*(000) = 708; colorless crystals, dimensions 0.25  $\times$  0.30  $\times$  0.25 mm<sup>3</sup>.

**Data Collection.** Nicolet single-crystal X-ray diffractometer (now P<sub>4</sub> system of Bruker),  $\theta - 2\theta$  scan technique, graphite-monochromated Cu K $\alpha$  ( $\lambda = 1.54178$  Å) radiation; 3399 reflections were measured ( $3.50 < \theta < 135^\circ$ ,  $1 \leq h \leq 12$ ,  $-1 \leq k \leq 14$ ,  $-13 \leq l \leq 12$ ), 2970 were unique. Three standard reflections were measured after every 97 reflections, which showed no significant decay.

**Structure Analysis and Refinement.** The crystal structure was solved by direct methods and refined by full-matrix least-squares on  $F^2$  values.<sup>20,21</sup> Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included at calculated positions and refined in the riding model. The final values of the residual  $R$  and  $wR_2$  [for 2970 reflections with  $I > 2\sigma(I)$ ] were 0.0482 and 0.1368, respectively. In the final difference Fourier synthesis, the electron density fluctuated in the range of 0.436 to  $-0.191$  eÅ<sup>-3</sup>.

**3'-Methoxyacoforestinine (2):** obtained as amorphous solid (19.7 mg);  $[\alpha]_D^{25}$  37° ( $c$  0.03, MeOH); UV (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 260 (4.91), 218 (5.20), 207 (5.20) nm; IR (CHCl<sub>3</sub>)  $\nu_{\max}$  3610–3795 (OH), 3215 (aromatic C–H), 1725, 1733 (C=O), 1601 (C=C) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.70 (1H, dd,  $J_{6',5'} = 8.5$  Hz,  $J_{6',2'} = 2.0$  Hz, H-6'), 7.62 (1H, d,  $J_{2',6'} = 2.0$  Hz, H-2'), 6.87 (1H, d,  $J_{5',6'} = 8.5$  Hz, H-5'), 4.81 (1H, d,  $J_{14\beta,9} = 5.0$  Hz, H-14 $\beta$ ), 3.92, 3.91, 3.53, 3.29, 3.25, 3.24 (each 3H, s, 6  $\times$  OCH<sub>3</sub>), 1.13 (3H, t,  $J_{21,22} = 7.1$  Hz, N–CH<sub>2</sub>–CH<sub>3</sub>), 0.56 (3H, t,  $J = 7.0$  Hz, O–CH<sub>2</sub>–CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  166 (OCOAr), 152.8 (C-4'), 148.5 (C-3'), 123.7 (C-6'), 123.3 (C-1'), 112.3 (C-2'), 110.2 (C-5'), 84.0 (C-16), 83.0 (C-1), 82.4 (C-6), 79.1 (C-14), 78.3 (C-8), 76.9 (C-18), 75.2 (C-13), 71.6 (C-3), 61.2 (C-17), 58.6 (OCH<sub>2</sub>–CH<sub>3</sub>), 59.1, 58.8, 58.7, 55.97, 55.84, 55.81 (s, 6  $\times$  OCH<sub>3</sub>), 50.8 (C-11), 48.8 (C-5), 48.6 (C-19), 47.8 (N–CH<sub>2</sub>–CH<sub>3</sub>), 45.8 (C-9), 45.7 (C-7), 43.1 (C-4), 41.3 (C-10), 37.7 (C-15), 35.5 (C-12), 33.0 (C-2), 15.2 (OCH<sub>2</sub>–CH<sub>3</sub>), 13.0 (N–CH<sub>2</sub>–CH<sub>3</sub>); EIMS  $m/z$  675 [M]<sup>+</sup> (3), 606 [M – CH<sub>3</sub>]<sup>+</sup> (3), 644 [M – OCH<sub>3</sub>]<sup>+</sup> (100), 630 (17), 165 (20); HREIMS  $m/z$  675.3612 (calcd for C<sub>36</sub>H<sub>53</sub>NO<sub>11</sub>).

**Acetylcholinesterase Inhibition Assay.** Acetylcholinesterase (Sigma Cat. No. 3389, Type VI-S: from electric eel) inhibition was determined spectrophotometrically using acetylthiocholine (Sigma Cat. No. A-5751) as substrate by modifying the method of Ellman et al.<sup>18</sup> The reaction was carried out in 100 mM sodium phosphate buffer at pH 8.0 at 25 °C. In a typical assay, 140  $\mu$ L buffer, 20  $\mu$ L enzyme preparation, and 20  $\mu$ L test compound solution were mixed and incubated for 30 min. 5,5'-Dithiobis-2-nitrobenzoic acid (DTNB, 10  $\mu$ L) was added, and then the reaction was initiated by adding 10  $\mu$ L of acetylthiocholine. The hydrolysis of acetylthiocholine was determined by monitoring the formation of the yellow 5-thio-2-nitrobenzoate anion as a result of the reaction of DTNB with thiocholine released by the enzymatic hydrolysis of acetylthiocholine at a wavelength of 412 nm. The concentration of the test compound that inhibited the enzyme

activity by 50% (IC<sub>50</sub>) was determined by interpolation using increasing levels of these substances in the assays.

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## References and Notes

- Pelletier, S. W.; Moody, N. V.; Joshi, B. S.; Schram, L. C. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1984; Vol. 2, pp 205–462.
- Baqar, S. R. *Medicinal and Poisonous Plants of Pakistan*; Printas: Karachi, 1989; p 8.
- Chopra, R. N.; Nayar, S. L.; Chopra, I. C. *Glossary of Indian Medicinal Plants*; CSIR: New Delhi, 1956.
- Benn, M. H.; Jacyno J. M. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1983; Vol. 1, pp 153–210.
- Wang, H.; Lao, A. *Heterocycles* **1985**, 23, 803–807.
- Singh, N.; Bajwa, G. S.; Singh, M. G. *J. Indian Chem. Soc.* **1966**, 4, 39–42.
- (a) Pelletier, S. W.; Naresh, V. M.; Puri, H. S. *Phytochemistry* **1977**, 16, 623–624. (b) Pelletier, S. W.; Naresh, V. M.; Puri, H. S. *J. Chem. Soc., Chem. Commun.* **1977**, 12–13.
- Desai, H. K.; Joshi, B. S.; Pelletier, S. W. *Heterocycles* **1986**, 24, 1061–1066.
- Desai, H. K.; Pelletier, S. W. *Heterocycles* **1989**, 29, 225–230.
- Pelletier, S. W.; Joshi, B. S.; Glinski, J. A.; Chokshi, H. P.; Chen, S. Y.; Bhandary, K.; Go, K. *Heterocycles* **1987**, 25, 365–376.
- Konno, C.; Shirasaka, M.; Hikino, H. *J. Nat. Prod.* **1982**, 45, 128–133.
- Bando, H.; Wada, K.; Amiya, T.; Kobayashi, K.; Fujimoto, Y.; Sakurai, T. *Heterocycles* **1987**, 26, 2623–2637.
- Wada, K.; Bando, H.; Mori, T.; Wada, R.; Kanaiwa, Y.; Amiya, T. *Chem. Pharm. Bull.* **1985**, 33, 3658–3661.
- Gonzalez, A. G.; De La Fuente, G.; Diaz, R.; Jones, P. G.; Sheldrick, G. M. *Tetrahedron Lett.* **1983**, 24, 959–960.
- Sultankhodzhaev, M. N.; Yunusov, M. S.; Yunusov, S. Yu. *Khim. Prir. Soedin.* **1973**, 199–205.
- Buckingham, J., Ed. *Dictionary of Natural Products*; Chapman & Hall: London, 1994; Vol. 3, p 3112.
- Ding, L.; Chen, Y.; Wu, F. *Planta Med.* **1991**, 57, 275–277.
- Pascual, de T. J. *An. Quim.* **1978**, 74, 311–313.
- Nodri, S.; Asakawa, N.; Sato, T. *Biol. Pharm. Bull.* **1995**, 18, 1145–1147.
- Sheldrick, G. M. SHELXTL, Version 5; Bruker, Analytical X-ray Systems, Inc.: Madison, WI, 1997.
- Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center (University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK).
- Ellman, G. L.; Courtney, D.; Andres, V.; Featherstone, R. M. *Biochem. Pharmacol.* **1961**, 7, 88–95.

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