Phytochemistry, Vol. 22, No. 9, pp. 2095–2096, 1983.
Printed in Great Britain.

0031–9422/83 $3.00 + 0.00

A 2-QUINOLONE ALKALOID FROM *ALMEIDEA GUYANENSIS*

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(*Revised received* 21 *January* 1983)

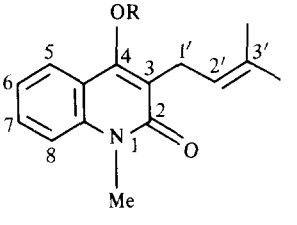
Key Word Index—*Almeidea guyanensis*; Rutaceae; bark; 2-quinolone/4-quinolone alkaloids; *N*-methylatanine; *N*-methylflindersine; *N*-methylkhaplofoline; almeine; 4-isopropenyl-*N*-methyl-3,4-dihydrofuro-2-quinolone; 4-demethyl-*N*-methylatanine.

Abstract—From *Almeidea guyanensis*, besides *N*-methylatanine, *N*-methylflindersine, *N*-methylkhaplofoline and 4-demethyl-*N*-methylatanine, a new 2-quinolone, almeine, has been isolated and its structure elucidated as 4-isopropenyl-*N*-methyl-3,4-dihydrofuro-2-quinolone.

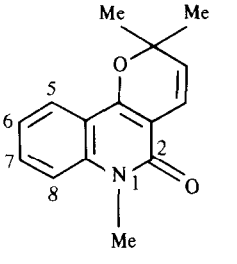
We have previously reported flavonoids from *Almeidea guyanensis* [1]. The present paper describes the isolation and identification of alkaloids present in crude extracts of stem and root barks.

Column chromatography of methanolic extracts of stem and root barks yielded four 2-quinolones (**1**–**4**) and one 4-quinolone (**5**). *N*-Methylatanine (**1**), *N*-methyl flindersine (**2**), *N*-methyl khaplofoline (**5**) and 4-demethyl-*N*-methylatanine (**3**) were identified by comparison with published spectral data [2–9]. *N*-Methylkhaplofoline [8, 9] and 4-demethyl-*N*-methylatanine [6], available by synthesis, have not been reported previously as natural products.

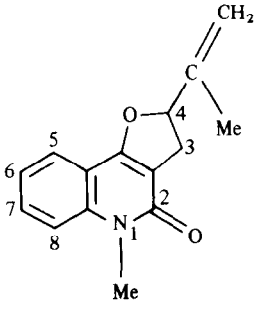
The complex UV spectra of **4** showed no shift on



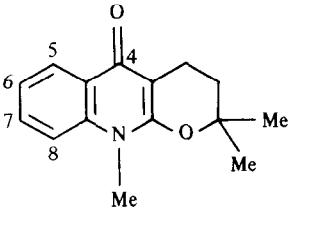
1 (*N*-Methylatanine) R=Me
3 (4-Demethyl-*N*-methyl atanine) R=H



2 (*N*-Methylflindersine)



4 (4-Isopropenyl-*N*-methyl-3,4-dihydrofuro-2-quinolone)



5 (*N*-Methylkhaplofoline)

addition of hydrochloric acid and the IR spectrum (1640, 1610 and 1590 cm^{-1}) was typical of 2-quinolone [10, 11]. ^1H NMR ($CDCl_3$) spectra exhibited a signal at δ 7.78 typical of 2-quinolone [10]. Mass spectral fragmentation is in accordance with cyclized 2-quinolone. The prominent peak (27%) $[M-41]^+$ indicated the presence of an isopropenyl side chain. ^1H NMR exhibited a multiplet of two protons at δ2.87–3.56 (asymmetric protons Ha and Hb) of the dihydrofuran nucleus bonded to H-4 (δ 5.42, *t*). Irradiation of this triplet confirmed the coupling. The ^1H NMR spectrum also exhibited resonance at δ 4.96 and 5.40 (2*s*, C=CH_2) [12, 13], 1. 78 (*s*, Me) and four aromatic protons (δ 7.11–7.82, *m*). These results showed that the structure of **4** was 4-isopropenyl-*N*-methyl-3,4-dihydrofuro-2-quinolone which we have named almeine.

EXPERIMENTAL

Air-dried stem and root barks of *A. guyanensis* Pulle collected in French Guyana were finely cut and extracted with MeOH. Extracts were concd under red. pres. and chromatographed on an XAD2 Amberlite column with MeOH as solvent.

Stem alkaloids were isolated on an Al_2O_3 (activity I) column. Compound **1** was eluted with C_6H_6–Et_2O (47 : 3) and purified by prep. TLC on Al_2O_3 with C_6H_6–Et_2O (1 : 1). Compound **2** was eluted with C_6H_6–Et_2O (1 : 1) and purified by prep. TLC on Si gel with CH_2Cl_2–MeOH (49 : 1). Compound **4** and **5** were eluted with Et_2O–MeOH (49:1) and purified with the same solvent.

Root alkaloids were eluted from the XAD2 Amberlite column with MeOH and separated into two fractions of different polarities. Chromatography of the most polar alkaloids on a Si gel column (CH_2Cl_2–MeOH, 98 : 3) yielded a major alkaloid (**3**). The less polar alkaloids (**1**, **2**, **4**) were isolated on an Al_2O_3 column (activity I) with *n*-hexane–$CHCl_3$ (17 : 8), then purified by prep. TLC on Si gel (CH_2Cl_2–MeOH, 9 : 1).

N-Methylatanine (**1**). Needles from MeOH, mp 130° (lit. 130° [2, 3]). UV and IR spectra identical with published data [2, 3]. MS *m/z* (rel. int.): 257 $[M]^+$ (75) ($C_{10}H_{19}NO_2$), 242 $[M-15]^+$ (80), 228 $[M-29]^+$ (25), 226 $[M-31]^+$ (30), 214 $[M-43]^+$ (100), 202 $[M-55]^+$ (80), 200 $[M-57]^+$ (25), 188 $[M-69]^+$ (40), 172 $[M-85]^+$ (50). ^1H NMR: δ 1.67, 1.79 (2 × 3H, 2*d*, *J* = 1 Hz, C=$\underline{Me}_2$), 3.38 (2H, *d*, *J* = 7 Hz, –$\underline{CH}_2$–CH=), 3.70 (3H, *s*, N-Me-1), 3.87 (3H, *s*, OMe-4), 5.22 (1H, *m*, –$\underline{CH}$=C=), 7.17, 7.35, 7.42 (3H, *m*, H-6–H-8), 7.73 (1H, *m*, H-5) typical of 2-quinolone.

N-Methylflindersine (**2**). Needles from MeOH, mp 84° (lit. 83–85° [7]). UV λ_{max}^{MeOH} nm: 226, 235, 333, 348, 358. IR spectra identical with published data [7]. MS *m/z* (rel. int.): 241 $[M]^+$ (25) ($C_{15}H_{15}NO_2$), 227 $[M-14]^+$ (20), 226 $[M-15]^+$ (100). ^1H NMR: δ 1.51 (6H, *s*, 2,2-dimethylchromene), 3.67 (3H, *s*, N-Me), 5.50, 6.68 (2 × 1H, 2*d*, *J* = 10 Hz), 7.06–8.0 (four aromatic protons, *m*, H-5–H-8) signal of H-5 at 7.91 typical of 2-quinolone.

4-Demethyl-N-methyl atanine (**3**). Needles from Et_2O, mp 164° (lit. 162–163° [4, 6]). UV λ_{max}^{MeOH} nm (log ε): 278 (3.89), 286 (3.89), 318 (3.86). IR spectra identical with published data [4]. MS *m/z* (rel. int.) 243 $[M]^+$ (46) ($C_{15}H_{17}NO_2$), 228 $[M-15]^+$ (17), 214 $[M-29]^+$ (10), 200 $[M-43]^+$ (100), 188 $[M-55]^+$ (50). ^1H NMR: δ 1.78, 1.82 (6H, 2*d*, *J* = 1 Hz) (*gem*-Me), 3.48 (2H, *d*, *J* = 7 Hz, $\underline{CH}_2$–CH=), 3.69 (3H, *s*, N-Me), 5.35 (1H, *m*, *J* = 7 Hz, HC=C), 7.13–7.46 (three aromatic protons, *m*, H-6–H-8), signal of H-5 at 7.88 (1H, *dd*, *J* = 7 and 2 Hz) typical of 2-quinolone. Methylation with CH_2N_2 yielded *N*-methylatanine.

4-Isopropenyl-N-methyl-3,4-dihydrofuro-2-quinolone (**4**). Could not be crystallized. UV λ_{max}^{MeOH} nm: 232, 284, 295, 319, 332. IR ν_{max}^{KBr} cm^{-1}: 2930, 2940, 1640 (2-quinolone) 1610, 1590. MS *m/z* (rel. int.): 241 $[M]^+$ (73) ($C_{15}H_{15}NO_2$), 226 $[M-15]^+$ (100), 224 $[M-17]^+$ (24), 212 $[M-29]^+$ (17), 200 $[M-41]^+$ (27), 198 $[M-43]^+$ (24). ^1H NMR: δ 1.78 (3H, *s*, Me), 2.87–3.56 (2H, *m*, H-3), 3.67 (3H, *s*, N-Me), 4.96, 5.11 (2H, 2*s*, =CH_2), 5.41 (1H, *t*, *J* = 10 Hz, H-4), 7.11–7.67 (three aromatic protons, *m*, H-6–H-8), 7.78 (one aromatic proton, *dd*, *J* = 9, 2 Hz, H-5) typical of angular cyclization of the furan ring (2-quinolone) [10].

N-Methyl khaplofoline (**5**). Needles from Et_2O, mp 119–120° (lit. 120–121° [8]). UV λ_{max}^{MeOH} nm: 237, 316, 327. IR spectra identical with published data [9]. MS *m/z* (rel. int.): 243 $[M]^+$ (65) ($C_{15}H_{17}NO_2$), 228 $[M-14]^+$ (15), 214 $[M-29]^+$ (20), 200 $[M-43]^+$ (95), 188 $[M-55]^+$. ^1H NMR: δ 1.45 (6H, *s*, 2Me), 1.85 (2H, *t*, $\underline{CH}_2$–C–Me_2), 2.77 (2H, *t*, Ar-CH_2), 3.69 (3H, *s*, N-Me), 7.20–8.47 (four aromatic protons, *m*, H-5–H-8) (signal of H-5 at 8.47 typical of 4-quinolone).

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