Simple efficient synthesis of pyranoquinoline alkaloids: flindersine, khaplofoline, haplamine and their analogues

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An efficient two step synthesis of pyranoquinoline alkaloids is described. Direct treatment of isoprene with 4-hydroxyquinolin-2(1*H*)-one in the presence of polyphosphoric acid furnished dihydroflindersine in good yield, and which on dehydrogenation led to a new synthesis of flindersine. Khaplofoline, a linear pyranoquinoline alkaloid, was obtained as a minor product. The syntheses of derivatives are also documented.

Keywords: isoprene, 4-hydroxyquinolin-2(1*H*)-one, PPA, DDQ

The last few decades have seen a significant rise in the phytochemical exploration of *Rutaceous species*, which produce more than 130 quinoline alkaloids including furo-, pyrano- and prenylquinolines. Flindersine[1] and *N*-methylflindersine[2] were isolated from the same species. Yunusov and his collaborators isolated the alkaloids khaplofoline[3a] and haplamine[3b,c] from the genus *Haplophyllum*.

Significance of flindersine, N-methylflindersine and haplamine

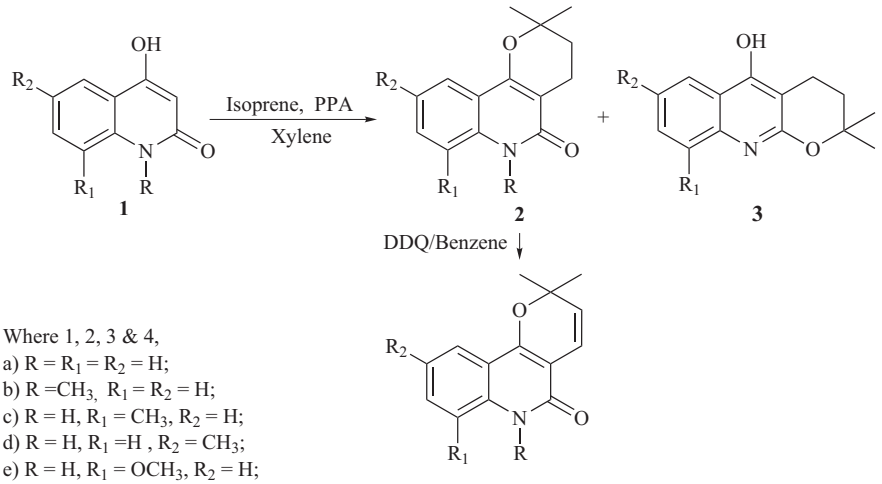
Recently, it has been reported[4] that haplamine and flindersine showed excellent cytotoxic activities. Flindersine is important due to its antifungal activity[5,6] and photoactivity in photochemotherapy,[7] whilst *N*-methylflindersine is reported to be an insect antifeedant principle of *Fagara chalybaea, F. holstii* and *Xylocarpus granatum*. Haplamine shows selective inhibition[6] against the odor-producing cyanobacterium. Based on the wide range of biological activities of these pyranoquinoline alkaloids, we have also synthesised some derivatives.

A number of methods for the synthesis of 2,2-dimethyl-pyranoquinoline alkaloids have been reported[8] since their isolation. Flindersine and its *N*-methyl derivative were synthesised by treatment of 4-hydroxy-*N*-methyl-3-prenylquinolin-2(1*H*)-one with DDQ,[9] or from the 3-isoprenyl-2,4-dimethoxyquinoline epoxides by treatment with potassium hydroxide in aqueous dimethylsulfoxide.[10] Lee *et al.*[11] synthesised these alkaloids with moderate yields by a ytterbium(III)triflate-catalysed reaction of 4-hydroxy-quinolin-2(1*H*)-one using a variety of α,β-unsaturated aldehydes. Khaplofoline was synthesised, either on oxidative cyclisation of 4-hydroxy-3-(3'-methylbut-1'-enyl)quinolin-2(1*H*)-one with DDQ[12] or the Prevost reaction of 3-prenyl-2-quinolones.[13] All these synthetic routes require several steps and are costly.

Over the last two decades, our laboratory has been involved in synthesising these alkaloids.[14] Recently we have reported[15] the synthesis of flindersine *via* (4 + 2) cycloaddition reaction using quinone methides.

Results and discussion

In this context, we have followed a simple and efficient two-step procedure for deriving both linearly and angularly fused pyranoquinoline alkaloid systems. To the best of our knowledge, there has been no report on the direct reaction of isoprene with quinolines. We used isoprene, which might act as a diene, with 4-hydroxyquinolin-2-one in the presence of PPA in xylene. Isoprene might have attached at C_3-position of the compound **1a** which resulted in angularly cyclised product **2a** (dihydroflindersine) in good yield with the small amount of linearly cyclised product **3a** (khaplofoline). The linear cyclisation is not favoured due to shortening of the corresponding N–C=O bond length and it less susceptible to reaction. The dihydroflindersine is subjected for dehydrogenation using DDQ. Thus, we synthesised the alkaloid flindersine(**4a**) with the overall yield of 57% (Scheme 1). Further, we have extended it to synthesise its



Where 1, 2, 3 & 4,
a) R = R_1 = R_2 = H;
b) R =CH_3, R_1 = R_2 = H;
c) R = H, R_1 = CH_3, R_2 = H;
d) R = H, R_1 =H , R_2 = CH_3;
e) R = H, R_1 = OCH_3, R_2 = H;
f) R = H, R_1 = H, R_2 = OCH_3; (4f: HAPLAMINE)

Scheme 1

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analogues for the simple reason that they might also attract pharmacological value.

Conclusion

We have developed a facile route to pyranoquinolone alkaloids using PPA catalysed reaction of 2,4-dihydroxyquinolines with isoprene as the key step. Since relatives of these two starting compounds are conveniently available, the present protocol allowed us assembling a wide range of pyranoquinoline alkaloids/derivatives for biological evaluation.

Experimental

Thin layer chromatography was used to follow the progress of the reaction and purity of products. Melting points were determined on a Boetius Microheating Table (Japan) and Mettler-FP5 Melting apparatus and are uncorrected. IR spectra were recorded in Shimadzu–8201 FT instrument (Japan) in KBr disc and only noteworthy absorption levels (reciprocal centimeter) are listed. ^{1}H & ^{13}C NMR spectra were recorded in Bruker-300 and 75 MHz spectrometer in $CDCl_3$ solution; Chemical shifts are expressed in ppm (δ) relative to TMS. Satisfactory microanalyses were obtained on Vario EL-III CHN analyser(Germany). Mass spectra were recorded on a Jeol-300 mass spectrometer(70eV) (Japan). DDQ and isoprene were purchased from Aldrich and Acros Organics respectively and used as received.

General procedure

Synthesis of dihydropyranoquinoline alkaloids (**2** and **3**): Equal moles of 4-hydroxy-1-methylquinolin-2(1*H*)-one (3 mmol) (**1a**) and isoprene (3 mmol) with polyphosphoric acid (approximately 2–3 g) in xylene (40 ml) were mechanically stirred at room temperature for 2 h and then heated at 145°C for 6 h with cold water circulation. Further 2 mmol of isoprene was added and heated for about 2 h. After completion of reaction, inferred through TLC, the xylene was distilled off and the crude reaction mixture was poured into 300 g of crushed ice and extracted with ethyl acetate. The organic layer was washed successively with saturated aq. sodium carbonate solution (2 × 20 ml) and then brine and dried over anhydrous sodium sulfate and concentrated. Column chromatography (silica gel 60–120 mesh) of the residue using a gradient mixture of petroleum ether and ethylacetate afforded dihydroproducts (**2** and **3**). Same procedure was applied for the derivatives **1b–f**.

Synthesis of flindersine and its analogues

A mixture of **2a** (1 mmol), and DDQ (1 mmol) in benzene (50 ml) was refluxed for 12 h. The solution was then evaporated to dryness. The residue was taken in ethyl-acetate and washed successively with aq. sodium carbonate (10%) and water. The combined organic extracts when subjected to silica gel column chromatography (PE: EtOAc = 80: 20) gave the desired product **4a**.The same was extended to derivatives **4b–f**.

2,2-Dimethyl-3,4-dihydropyrano[3,2-c]quinolin-5(6H)-one (**2a**) *(dihydroflindersine)*: M.p. 232°C; yield 67%; IR (KBr, ν_{max}) cm^{-1} 1640, 3248; ^{1}H NMR ($CDCl_3$) δ/ppm: 1.43(6H, s, 2 × CH_3), 1.65(2H, t, J = 6.40 Hz, C_3–CH_2), 2.34 (2H, t, J = 6.40 Hz, C_4–CH_2), 7.1–7.9(4H, m, Ar–H), 10.87(1H, bs, NH); ^{13}C NMR($CDCl_3$) δ/ppm 17.05(C_2–($\underline{C}H_3$)$_2$), 17.61(C_3), 26.70(C_4), 104.67($\underline{C}_2$–CH_3)$_2$), 116.46(C_{4a}), 122.93(C_8), 120.83(C_9), 121.59(C_{10}), 123.85(C_7), 130.42 (C_{10a}), 134.69(C_{6a}), 159.04(C_{10b}), 166.66(C=O); MS (*m/z*) 229; Analysis (%): Calcd. C 73.34, H 6.59, N 6.11; Found C 73.32, H 6.65, N 6.05 ($C_{14}H_{15}NO_2$).

2,2,6-Trimethyl-3,4-dihydropyrano[3,2-c]quinolin-5-one (**2b**): M.p. 176°C; yield 72%; IR(KBr, ν_{max}) cm^{-1}, 1668 cm^{-1}(C=O); ^{1}H NMR($CDCl_3$) δ/ppm 1.42(6H, s, 2 × CH_3), 1.62(2H, t, J = 6.60 Hz, C_3–CH_2), 2.35(2H, t, J = 6.60 Hz, C_4–CH_2), 3.83(3H, s, N–CH_3), 7.1–8.0(4H, m, Ar–H); ^{13}C NMR($CDCl_3$) δ/ppm: 17.07(C_2–($\underline{C}H_3$)$_2$), 17.67(C_3), 28.91(C_4), 37.22(N–$\underline{C}H_3$), 102.84($\underline{C}_2$–CH_3)$_2$), 117.36(C_{4a}), 120.32(C_8), 121.00(C_9), 122.16(C_{10}), 122.72 (C_7), 130.48 (C_{10a}), 137.88(C_{6a}), 159.37(C_{10b}), 167.94(C=O); MS (*m/z*) 243; Analysis (%): Calcd. C 74.05, H 7.04, N 5.76; Found C 74.41, H 7.22, N 5.83 ($C_{15}H_{17}NO_2$).

2,2,7-Trimethyl-3,4-dihydropyrano[3,2-c]quinolin-5(6H)-one (**2c**): M.p. 221°C, yield 64%; IR (KBr, ν_{max}) cm^{-1}1648 cm^{-1}(C=O), 3250; ^{1}H NMR ($CDCl_3$) δ/ppm: 1.42(6H, s, 2 × CH_3), 1.86(2H, t, J = 6.60 Hz, C_3–CH_2), 2.46(3H, s, C_7–CH_3), 2.65(2H, t, J = 6.60 Hz, C_4–CH_2), 7.09 (1H, t, J = 7.6 Hz, C_9–H), 7.30(1H, d, J = 7.6 Hz, C_8–H), 7.78(1H, d, J = 7.72 Hz C_{10}–H), 9.13(1H, bs, NH); ^{13}C NMR($CDCl_3$) δ/ppm: 17.25(C_2–($\underline{C}H_3$)$_2$), 17.54(C_3), 27.03(C_4), 32.32(C_7–$\underline{C}H_3$), 105.33($\underline{C}_2$–CH_3)$_2$), 116.20(C_{4a} and C_8), 120.90(C_9), 121.81(C_{10}), 128.72 ($\underline{C}_7$–CH_3), 131.51(C_{10a}), 135.67(C_{6a}), 158.02(C_{10b}), 164.31(C=O); MS (*m/z*) 243; Analysis (%): Calcd. C 74.05, H 7.04, N 5.76; Found C 74.32, H 7.21, N 5.78 ($C_{15}H_{17}NO_2$).

2,2,9-Trimethyl-3,4-dihydropyrano[3,2-c]quinolin-5(6H)-one (**2d**): M.p. 228°C, yield 62%; IR (KBr, ν_{max}) cm^{-1}1650 cm^{-1}(C=O), 3247; ^{1}H NMR ($CDCl_3$) δ/ppm: 1.41(6H, s, 2 × CH_3), 1.78(2H, t, J = 6.60 Hz, C_3–CH_2,), 2.45(3H, s, C_9–CH_3), 2.62 (2H, t, J = 6.60 Hz, C_4–CH_2), 7.31(1H, d, J = 7.2 Hz, C_8–H), 7.70(1H, s, C_{10}–H), 7.92(1H, d, J = 7.2 Hz, C_7–H), 9.45(1H, bs, NH); ^{13}C NMR($CDCl_3$) δ/ppm: 17.14(C_2–($\underline{C}H_3$)$_2$), 17.60(C_3), 26.78(C_4), 32.56(C_9–$\underline{C}H_3$), 107.00($\underline{C}_2$–CH_3)$_2$), 116.15(C_{4a}), 117.11(C_8), 128.08(C_9), 121.93(C_{10}), 122.68 ($\underline{C}_7$), 132.88(C_{10a}), 134.98(C_{6a}), 159.17(C_{10b}), 165.70(C=O); MS (*m/z*) 243; Analysis (%): Calcd. C 74.05, H 7.04, N 5.76; Found C 74.43, H 7.14, N 5.81 ($C_{15}H_{17}NO_2$).

2,2-Dimethyl-7-methoxy-3,4-dihydropyrano[3,2-c]quinolin-5(6H)-one (**2e**): M.p. 165°C; yield 61%; IR (KBr, ν_{max}) cm^{-1} 1652, 3230; ^{1}H NMR ($CDCl_3$) δ/ppm 1.52(6H, s, 2 × CH_3), 1.67(2H, t, J = 6.40 Hz, C_3–CH_2), 2.54(2H, t, J = 6.40 Hz, C_4–CH_2), 3.85(3H, s, C_7–OCH_3), 7.28–7.86(3H, m, Ar–H), 10.17(1H, bs, NH); ^{13}C NMR ($CDCl_3$) δ/ppm: 17.25 (C_2–($\underline{C}H_3$)$_2$), 17.59(C_3), 27.55(C_4), 56.56(C_7–O–$\underline{C}H_3$), 97.81($\underline{C}_2$–CH_3)$_2$), 115.23(C_{4a}), 119.87(C_8), 121.31(C_9), 123.58(C_{10}), 131.56(C_{10a}), 133.47($\underline{C}_7$–O–CH_3), 135.19(C_{6a}), 158.66(C_{10b}), 164.90(C=O); MS (*m/z*) 259; Analysis (%): Calcd. C 69.48, H 6.61, N 5.40; Found C 69.35, H 6.68, N 5.47 ($C_{15}H_{17}NO_3$).

2,2-Dimethyl-9-methoxy-3,4-dihydropyrano[3,2-c]quinolin-5(6H)-one (**2f**): M.p. 171°C; yield 63%; IR (KBr, ν_{max}) cm^{-1} 1667, 3210; ^{1}H NMR ($CDCl_3$) δ/ppm 1.49(6H, s, 2 × CH_3), 1.63(2H, t, J = 6.60 Hz, C_3–CH_2), 2.47(2H, t, J = 6.60 Hz, C_4–CH_2), 3.87(3H, s, C_9–OCH_3), 7.24–7.89(3H, m, Ar–H), 9.84(1H, bs, NH); ^{13}C NMR($CDCl_3$) δ/ppm: 16.98(C_2–($\underline{C}H_3$)$_2$), 17.45(C_3), 26.75(C_4), 58.91(C_9–O–$\underline{C}H_3$), 99.27($\underline{C}_2$–CH_3)$_2$), 117.36(C_{4a}), 120.32(C_8), 124.67(C_{10}), 127.41(C_7), 132.17(C_{10a}), 133.44($\underline{C}_9$–O–CH_3), 136.82(C_{6a}), 157.90(C_{10b}), 167.81(C=O); MS (*m/z*) 259; Analysis (%): Calcd. C 69.48, H 6.61, N 5.40; Found C 69.73, H 6.65, N 5.44 ($C_{15}H_{17}NO_3$).

Khaplofoline (**3a**): M.p. 272°C; yield 10%; Spectral data were identical with the earlier reported.[10,14]

2,2,10-Trimethyl-5-hydroxy-3,4-dihydropyrano[2,3-b]quinoline (**3b**): yield – Nil.

2,2,9-Trimethyl-5-hydroxy-3,4-dihydropyrano[2,3-b]quinoline (**3c**): M.p. 186°C, yield 6%; IR (KBr, ν_{max}) cm^{-1} 1610 cm^{-1}(C=N), 3425–3550(O–H); ^{1}H NMR($CDCl_3$) δ/ppm: 1.37(6H, s, 2 × CH_3), 1.48(2H, t, J = 6.40 Hz, C_3–CH_2), 2.26(3H, s, C_9–CH_3), 2.58(2H, t, J = 6.40 Hz, C_4–CH_2), 7.41(1H, t, J = 7.8 Hz, C_7–H), 7.62(1H, d, J = 7.76 Hz, C_8–H), 7.84(1H, d, J = 7.8 Hz, C_6–H), 10.17(1H, bs, OH); ^{13}C NMR($CDCl_3$) δ/ppm: 17.22(C_2–($\underline{C}H_3$)$_2$), 18.73(C_3), 29.55(C_4), 32.81(C_9–$\underline{C}H_3$), 110.64($\underline{C}_2$–CH_3)$_2$), 120.32(C_8), 121.06(C_7), 125.58(C_6), 128.86(C_{4a}), 129.17($\underline{C}_9$), 130.56(C_{5a}), 136.47(C_{9a}), 149.43(C_5), 171.57(C_{10a}); MS (*m/z*) 243; Analysis (%): Calcd. C 74.05, H 7.04, N 5.76; Found C 74.09, H 6.98, N 5.79 ($C_{15}H_{17}NO_2$).

2,2,7-Trimethyl-5-hydroxy-3,4-dihydropyrano[2,3-b]quinoline (**3d**): M.p. 228°C, yield 6%; IR (KBr, ν_{max}) cm^{-1} 1605 cm^{-1}(C=N), 3420–3550(O–H); ^{1}H NMR($CDCl_3$) δ/ppm: 1.38(6H, s, 2 × CH_3), 1.48(2H, t, J = 6.60 Hz, C_3–CH_2), 2.29(2H, t, J = 6.60 Hz, C_4–CH_2), 2.52(3H, s, C_7–CH_3), 7.21(1H, d, J = 8.0 Hz, C_8–H), 7.80(1H, s, C_6–H), 7.95(1H, d, J = 8.0 Hz, C_9–H), 10.0(1H, bs, OH); ^{13}C NMR($CDCl_3$) δ/ppm: 16.95(C_2–($\underline{C}H_3$)$_2$), 17.67(C_3), 27.06(C_7–$\underline{C}H_3$), 30.75(C_4), 103.81($\underline{C}_2$–CH_3)$_2$), 120.35(C_8), 125.48(C_6), 126.77 (C_9), 128.83(C_7), 129.96(C_{4a}), 130.56(C_{5a}), 138.42(C_{9a}), 149.21(C_5), 169.33(C_{10a}); MS (*m/z*) 243; Analysis (%): Calcd. C 74.05, H 7.04, N 5.76; Found C 74.29, H 7.11, N 5.83 ($C_{15}H_{17}NO_2$).

Flindersine (**4a**): M.p. 195°C; yield 85%; Spectral data were identical with earlier reported[1].

N-Methylflindersine (**4b**): M.p. 85°C; Yield 85%; IR (KBr, ν_{max}) cm^{-1} 1662, 3213; ^{1}H NMR($CDCl_3$) δ 1.45(s, 6H, 2 × CH_3), 3.66(s, 3H, N–CH_3), 5.87(d, 1H, C_3–H, J = 6.42 Hz), 6.8–7.8(m, 5H, Ar–H & C_4–H); MS (*m/z*) 241; Analysis (%): Calcd. C 74.67, H 6.27, N 5.80; Found C 74.70, H 6.22, N 5.84 ($C_{15}H_{15}NO_2$).

7-Methylflindersine (**4c**): M.p. 189°C, yield 85%, IR(KBr, ν_{max})cm^{-1} 1651(C=O), 3220(NH); ^{1}H NMR ($CDCl_3$) δ/ppm: 1.41(s, 6H, 2 × CH_3), 2.44(s, 3H, C_7–CH_3), 5.83(d, 1H, C_3–H, J = 6.4 Hz), 6.80(d, 1H, C_4–H, J = 6.4 Hz), 7.11(t, 1H, C_9–H, J = 7.96 Hz), 7.35(d, 1H, C_8–H, J = 8.0 Hz), 7.80(d, 1H, C_{10}–H, J = 8.0 Hz), 9.10(bs, 1H, NH); ^{13}C NMR($CDCl_3$) δ/ppm: 19.31(C_2–($\underline{C}H_3$)$_2$), 30.09(C_7–$\underline{C}H_3$), 115.90($\underline{C}_2$–(CH_3)$_2$), 132.78(C_3), 118.35(C_8), 120.33(C_4), 121.23(C_9), 124.75(C_{10}), 126.35(C_{4a}), 128.84($\underline{C}_7$–CH_3), 130.78(C_{10a}), 141.32(C_{6a}), 155.68(C_{10b}), 164.73(C=O); MS (*m/z*) 241; Analysis (%): Calcd. C 74.67, H 6.27, N 5.81; Found C 74.72, H 6.30, N 5.79 ($C_{15}H_{15}NO_2$).

9-Methylflindersine (**4d**): M.p. 176°C, yield 90%, IR (KBr, ν_{max}) cm^{-1}1660(C=O), 3224(NH); ^1H NMR ($CDCl_3$) δ/ppm: 1.40(s, 6H, 2 × CH_3), 2.35(s, 3H, C_9–CH_3), 5.76(d, 1H, C_3–H, *J* = 6.80 Hz), 6.53(d, 1H, C_4–H, *J* = 6.80 Hz), 7.44(d, 1H, C_8–H, *J* = 7.8 Hz), 7.90(d, 1H, C_7–H, *J* = 7.8 Hz), 7.80(s, 1H, C_{10}–H), 9.18(bs, 1H, NH); ^{13}C NMR($CDCl_3$) δ/ppm: 20.07(C_2–($\underline{C}H_3$)$_2$), 29.26(C_9–$\underline{C}H_3$), 116.77($\underline{C}_2$–CH_3)$_2$), 117.10(C_8), 131.09(C_3), 126.14(C_{10}), 126.34(C_7), 126.53($\underline{C}_4$), 128.50($\underline{C}_9$–CH_3), 128.61(C_{4a}), 133.06(C_{10a}), 136.00(C_{6a}), 150.41(C_{10b}) 164.98(C=O); MS (*m/z*) 241; Analysis (%): Calcd. C 74.67, H 6.27, N 5.81; Found C 74.67, H 6.29, N 5.81 ($C_{15}H_{15}NO_2$).

7-Methoxyflindersine (**4e**): M.p. 180°C; Yield 82%; IR (KBr, ν_{max}) cm^{-1} 1660(C=O), 3265(NH); ^1H NMR ($CDCl_3$) δ/ppm: 1.47(s, 6H, 2 × CH_3), 3.91(s, 3H, –OCH_3), 5.82(d, 1H, C_3–H, *J* = 6.2 Hz), 6.76(d, 1H, C_4–H, *J* = 6.2 Hz), 11.03 (s, 1H, NH), 7.2–7.8(m, 3H, Ar–H); ^{13}C NMR ($CDCl_3$) δ/ppm: 20.78(C_2–($\underline{C}H_3$)$_2$), 56.87(C_7–O–$\underline{C}H_3$), 117.20($\underline{C}_2$–CH_3)$_2$), 118.45(C_8), 120.25(C_4), 121.73(C_9), 125.49(C_{10}), 128.31(C_{4a}), 130.80(C_{10a}), 134.45(C_3), 136.83(C_7), 138.64(C_{6a}), 160.01(C_{10b}), 168.52(C=O); MS (*m/z*) 257; Analysis (%): Calcd. C 70.02, H5.88, N 5.44; Found C 70.14, H 5.86, N 5.47 ($C_{15}H_{15}NO_3$).

9-Methoxyflindersine (**4f**) *(Haplamine)*: M.p. 210°C; Yield 80%; IR (KBr, ν_{max})cm^{-1} 1656(C=O), 3215(NH); ^1H NMR ($CDCl_3$) δ/ppm 1.47(s, 6H, 2 × CH_3), 3.90(s, 3H, C_9–OCH_3), 5.34(d, 1H, C_3–H, *J* = 6.20 Hz), 6.71(d, 1H, C_4–H, *J* = 6.20 Hz), 7.30–7.95(m, 3H, Ar–H), 9.58(bs, 1H, NH); ^{13}C NMR($CDCl_3$) δ/ppm: 19.42(C_2–($\underline{C}H_3$)$_2$), 57.71(C_9–O–$\underline{C}H_3$), 118.09($\underline{C}_2$–CH_3)$_2$), 120.32(C_8), 124.57(C_{10}), 125.91(C_4), 127.40(C_7), 129.34(C_{4a}), 131.04(C_{10a}), 131.67(C_3), 137.82($\underline{C}_9$–O–CH_3), 141.22(C_{6a}), 152.43(C_{10b}), 166.71(C=O); MS (*m/z*) 257; Analysis (%): Calcd. C 70.02, H 5.88, N 5.44; Found C 70.23, H 5.93, N 5.51 ($C_{15}H_{15}NO_3$).

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References

1 (a) H. Mathes, E. Schreiber, *Ber dert pharm ges*, 1914, **24**, 385; (b) R.F.C. Brown, J.J. Hobbs, G.K. Hughes and E. Ritchie, *Aust. J. Chem.,* 1954, **7**, 348; (c) A.V. Robertson, *Aust. J. Chem.,* 1963, **16**, 451; (d) D. Lavie, N. Danieli, R. Weitman and E. Glotter, *Tetrahedron*, 1968, **24**, 3011; (e) M.A. Munoz, M.R. Torres, B.K. Cassels, *J. Nat. Prod.*, 1982, **45**, 367; (f) A. Ulubelen, *Phytochemistry*, 1984, **23**, 2123; (g) S. Ahmad, *J. Nat. Prod.,* 1984, **47**, 391, (h) S. Mitaku, A.L. Skaltsounis, F. Tillequin and M. Koch, *J. Nat. Prod.,* 1985, **48**, 772.

2 (a) F.Y. Chou, K. Hostettmann, I. Kubo, K. Nakanishi and M. Taniguchi, *Heterocycles*, 1977, **7**, 969; (b) K. Hostettmann, M.J. Pettei, I. Kubo and K. Nakanishi, *Helv. Chim. Acta* 1977, **60**, 670; (c) L. Jurd, R.Y. Wong, *Aust. J. Chem.* 1981, **34**, 1625; (d) C. Moulis, K.R. Wira sutisna, J. Gleye, P. Loiseau, E. Stanislas and C. Moretti, *Phytochemistry,* 1983, **22**, 2095.

3 (a) I.M. Fakhrutdinova, G.P. Sidyakin and S.Yu.Yunusov, *Uzbeksk. Khim. Zhur.*, 1963, **7**, 41; (b) V.I. Akhmedzhanova, I.A. Bessonova and S. Yu. Yunusov, *Khim. Prir. Soedin.* 1974, 109; (c) V.I. Akhmedzhariova, I.A. Bessonova and S. Yu. Yunusov, *Chemistry of Natural compounds*, 1975, **10**, 121; (d) M.S. Hifnawy, J. Vaquette, T. Sevenet, J.L. Povsset and A. Cave, *Planta Med.*, 1976, **29**, 346; (e) C.L. Cantrell, K.K. Schrader, L.K, Mamonov, G.T. Sitpaeva, T.S. Kustova, C. Dunbar and D.E. Wedge, *J. Agric. Food Chem.*, 2005, **53**, 7741.

4 O. Jansen, M. Frederich, M. Tits, L. Angenot, A. Chariot, E. Ollivier, G. Balansard and V. Akhmedjanova, *Symposium on Plants in Health and Culture* held on February 16-17, 2004, Leiden University Leiden, Netherland.

5 M. Rahmani, C.Y. Ling, S. Meon, H.B.M. Ismail and M.A. Sukari, *Pharmaceut. Biol. (Form. Intl. J. Pharmacognosy)*, 2004, **42**, 430.

6 C.L. Cantrell, K.K. Schrader, L.K. Mamonov, G.T. Sitpaeva, T.S. Kustova, C. Dunbar and D.E. Wedge *J. Agric. Food Chem.,* 2005, **53**, 7741.

7 F. Hanawa, *Planta Med,* 2004, **70**, 531.

8 (a) K.C. Anand, A.K. Sinha, *Ind. J. Chem. (Sect-B)*, 1991, **30B**, 560; (b) K.C. Anand, A.K. Sinha, *Ind. J. Chem. (Sect-B)*, 1991, **30B**, 604; (c) E.A. Clarke, M.F. Grundon, *J. Chem. Soc*., 1964, 4190; (d) R.F.C. Brown, J.J. Hobbs, G.K. Hughes and E. Ritchie, *Aust. J. Chem.,* 1956, **9**, 277; (e) P. Bravo, G. Resnati and F. Viani, *Gazz. Chim. Ital.* 1988, **118**, 507; (f) Ae. De. Groot and B.J.M. Jansen, *Tetrahedron Lett.,* 1975, **39**, 3407; (g) J.W. Huffman and T.M. Hsu, *Tetrahedron Lett*., 1972, **2**, 141.

9 M.F. Grundon, D.M. Harrison, M.G. Magee, M.J. Rutherford and S.A. Surgenor, *Proc. R. Ir. Acad.- Sect. B,* 1983, 83, 103.

10 M.R. Bowman, M.F. Grundon and K.J. James, *J. Chem. Soc., Perkin Trans 1*, 1973, 1055.

11 Y.R. Lee, H.I. Kweon, W.S. Koh, K.R. Min, Y. Kim and S.H. Lee, *Synthesis*, 2001, 1851.

12 F. Piozzi, P. Venturella and A. Bellino, *Gazz. Chim. Ital.*, 1969, **99**, 711.

13 M. Subramaniam, P.S. Mohan, P. Shanmugam and K.J. Rajendra Prasad, *Z.Naturforsch*, 1992, **47b**, 1016.

14 (a) M. Ramesh, V. Arisvaran, S.P. Rajendran and P. Shanmugam, *Tetrahedron Lett* 1982, **23**, 967; (b) M. Ramesh, P.S. Mohan and P. Shanmugam, *Tetrahedron*, 1984, **40**, 4041; (c) M. Sekar and K.J. Rajendra Prasad, *J. Nat. Prod.*, 1998, **61**, 294; (d) R.N. Kumar, S.T. Selvi, T, Suresh and P.S. Mohan, *Heterocycles*, 2002, **57**, 357.

15 R.N. Kumar, S.T. Selvi, T. Suresh and P.S. Mohan, *Ind. J. Chem. (Sect-B)*, 2003, **42B**, 187.