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Alkaloids from *Ruta montana*

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Abstract

Two known and four new quinoline and 4-quinolone type alkaloids were isolated from *Ruta montana* collected from Rommani (Morocco). The known compounds were 1-methyl-4-methoxy-2-quinolone and evolitrine. The structures of the new compounds were established from 1D and 2D NMR experiments including HMQC, HMBC and MS spectral methods as 2-(nonan-8-one)-(1H)-4-quinolone, 2-(nonan-8-one)-4-methoxy-quinoline, 2-(nonan-8-one)-*N*-methyl-4-quinolone and 2-(decan-9-one)-*N*-methyl-4-quinolone.

Keywords: *Ruta montana*; Rutaceae; New quinoline alkaloids; Quinolone alkaloids; 1-Me-4-OMe-2-quinolone; Evolitrine

1. Introduction

In previous studies with *Ruta montana* (L.) L. the presence of alkaloids (Vasudevan & Luckner, 1968; Ulubelen, 1990) and coumarins (Burges del Castillo, Rodriguez, Rodriguez & Secundino, 1985; Şener & Mutlugil, 1985) were shown. In the present study with the Morocco collection we have isolated six alkaloids two of which were known compounds 1-methyl-4-methoxy-2-quinolone (Nayar, Sutar & Bhan, 1971), and evolitrine (Baudouin, Tillequin, Koch, Pusset & Sevenet, 1981; Dreyer, 1980). The new compounds were 2-(nonan-8-one)-(1H)-4-quinolone (**1**), 2-(nonan-8-one)-4-methoxy-quinoline (**2**), 2-(nonan-8-one)-*N*-methyl-4-quinolone (**3**), 2-(decan-9-one)-*N*-methyl-4-quinolone (**4**).

2. Results and discussion

The UV spectra for compounds **1**, **3**, **4** showed typical 4-quinolone peaks at 330–332, 320, 235–236, 215–220 nm. The ^{1}H-NMR spectra of these three compounds correlated the quinolone structure with the broad doublet for **1** and double doublet for **3** and **4** signals at δ 8.35–8.48 corresponding to H-5 and indicating the presence of a carbonyl group at C-4. The HR-MS indicated the molecular formulae $C_{18}H_{23}NO_2$ (m/z 285.1832) for **1**, $C_{19}H_{25}NO_2$ (m/z 299.1976) for **3** and $C_{20}H_{27}O_2$ (m/z 313.2136) for **4**, all corresponding to eight degrees of unsaturation as double bond equivalent, of which two were accounted for by the bicyclic ring system, four for the double bonds, one for the carbonyl group and the remaining one for the carbonyl group on the side chain. The mass fragmentation of the three compounds **1**, **3**, **4** showed $[M\text{-}Me]^+$, $[M\text{-}COMe]^+$ and successive loss of ($-CH_2$) until base peaks m/z 173 for **3** and **4** and m/z 159 for **1** which indicated nonan-8-one side chain for **1** and **3** and decan-9-one for **4**. The ^{1}H-NMR spectrum showed the signals for the aliphatic side chain in all compounds as given in (Table 1).

The placement of the side chain was decided by HMBC experiment for compounds **1** and **2**. Due to the small amounts of compounds **3** and **4** ^{13}C-NMR spectra were not recorded, from the spectral similarities the side chain of **3** and **4** should also be placed

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Table 1
NMR data of compounds **1**–**4**

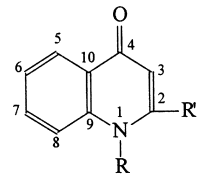
	1			**2**			**3**	**4**
	^{1}H	^{13}C	HMBC	^{1}H	^{13}C	HMBC	^{1}H	^{1}H
1	–	–		–	–		–	–
2	–	125.0 *s*		–	119.95		6.22	6.23
3	6.21 *s*	100.3 *d*	C-5, C-9, C-10	6.62 *s*	99.8 *d*	C-1, C-4, C-5, C-10	–	–
4	–	178.9 *s*		–	164.2 *s*		8.48 *dd*	8.43 *dd*
5	8.35 *brd*[a]	125.3 *d*	C-4, C-7, C-10	8.18 *brd*	121.5 *d*	C-7, C-9	7.38 *brt*	7.39 *brt*
6	7.32 *brt*	123.5 *d*		7.42 *brt*	124.8 *d*		7.68 *dt*	7.65 *dt*
7	7.58 *dt*	131.7 *d*		7.63 *dt*	129.7 *d*	C-9, C-8	7.50 *brd*	7.65 *brd*
8	7.72 *brd*	118.3 *d*	C-5, C-9, C-10	7.97 *brd*	128.2 *d*		–	–
9	–	154.7 *s*		–	149.6 *s*		–	–
10	–	140.5 *s*		–	162.3 *s*		–	–
OMe	–	–		4.05 *s*	55.6 *q*	C-4, C-10	–	–
NMe	–	–		–	–		3.74 *s*	3.73 *s*
1′	2.63 *t*	34.3 *t*		2.85 *t*	39.6 *t*	C-3, C-4	2.73 *t*	2.74 *t*
2′	1.70 *brs*	28.8 *t*		1.8 *m*	23.7 *t*		1.38 *m*	1.30 *brs*
3′	1.50 *brs*	28.8 *t*		1.6 *m*	30.1		1.60 *m*	1.30 *brs*
4′	1.20 *brs*	28.8 *t*		1.28 *m*	29.0		1.60 *m*	1.30 *brs*
5′	1.20 *brs*	28.8 *t*		1.30 *m*	29.3		1.38 *m*	1.30 *brs*
6′	1.20 *brs*	28.8 *t*		1.32 *m*	29.9		1.38 *m*	1.30 *brs*
7′	2.38 *t*	43.6 *t*		2.42 *t*	43.7		2.42 *t*	1.30 *brs*
8′	–	210.5 *s*		–	209.5		–	1.70 *t*
9′	2.1 *s*	29.8 *q*	C-6′, C-7′, C-9′	2.18 *s*	29.4	C-7′, C-8′	2.14 *s*	–
10′	–	–		–	–		–	2.30 *s*

[a] *J* (Hz): Compound **1**: 5, 6 = 7, 8 = 8; 1′, 2′ = 7, 4; 6′, 7′ = 7, 3; Compound **2**: 5, 6 = 7, 8 = 8; 6, 7 = 1.1, 8.0; 1′, 2′ = 7′, 6′ = 7, 5; Compound **3**: 5, 6 = 7, 8 = 1.1, 8; 5, 6 = 8; 1′, 2′ = 7, 3; 6′, 7′ = 7.2; Compound **4**: 5, 6 = 7, 8 = 1.3, 8; 1′, 2′ = 7, 4.

at C-2. From the HMQC and HMBC experiments the structure of **1** was assigned unambiguously as 2-(nonan-8-one)-(1H)-4-quinoline (**1**). The structure of **3** and **4** should be 2-(nonan-8-one)-*N*-methyl-4-quinoline (**3**), 2-(decan-9-one)-*N*-metyl-4-quinoline (**4**).

The molecular formula of the second new compound **2**, $C_{19}H_{25}NO_2$ calculated from its HR-MS (*m*/*z* 299.1978); indicated eight degrees of unsaturation, two of which were accounted for the bicyclic ring system, one for the carbonyl group on the side chain and the remaining five for the double bonds. The ^{1}H-NMR spectrum showed the chemical shift of the aromatic proton H-5 in a fairly lower field at δ 8.18 (1H, *brd*, *J* = 8 Hz, H-5) compared to those of other three compounds **1**, **3** and **4** indicated a quinoline structure. The chemical shift of the methoxy group at δ 4.05 an *O*-methyl rather than an *N*-methyl group correlated with the aromatic character of the ring system (Table 1).

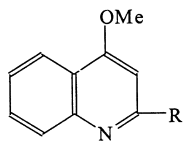
The IR spectrum showed the side chain carbonyl group at 1705 cm^{-1} and aromatic signals at 1595, 1565, 1510 cm^{-1}. The UV spectrum showed the presence of a conjugated aromatic system with the maxima at 312 (sh), 300 and 225 nm. The correlation of the protons and carbons were followed from the HMQC spectrum and unambiguous assignment of the molecule was possible from the HMBC experiment (Table 1). The spectral data showed the structure of compound **2** as 2-(nonan-8-one)-4-methoxy-quinoline.



1 R = H ; R' = $(CH_2)_7$ - CO- CH_3 (1′-7′, 8′, 9′)

3 R = Me ; R' = $(CH_2)_7$ - CO - CH_3 (1′-7′, 8′, 9′)

4 R = Me; R' = $(CH_2)_8$ - CO - CH_3 (1′-8′, 9′, 10′)



2 R = $(CH_2)_7$ - CO - CH_3 (1′-7′, 8′, 9′)

3. Experimental

3.1. General

UV: Shimadzu UV-160 A in MeOH. IR: Perkin-Elmer Model 983 in $CHCl_3$. ^{1}H- and ^{13}C-NMR in BrukerAC 200L instrument 200 and 50.32 MHz and for the 2D exp. 500 and 125 MHz, respectively with TMS as int. standard. HRMS: VG Zab Spec GC-MS spectrometer.

3.2. Plant material

The whole plant *Ruta montana* was collected from

Rommani, 80 km east of Rabat (Morocco), in August 1996 and identified by Prof. M. Fennane (Institut Scientifique, Rabat), a voucher specimen was deposited in the Herbarium of the same Institute.

3.3. Extraction and isolation

The plant material (300 g) (120 g leaves, 120 g fruits and 60 g roots) was extracted with $CHCl_3$ separately to yield 6, 6 and 2 g crude extracts, respectively. The TLC examination of the extracts indicated same alkaloids for the leaves and the fruits therefore they were combined to yield Frac. A; however the roots had different alkaloids and worked up separately as Frac. B. Both fractions A and B were dried, defatted with ether and then extracted with 2% HCl (20 × 10 ml), the acidic aqueous solution basified with NH_3 to bring pH 8–9 and extracted with $CHCl_3$ until extinction. The crude alkaloidal mixtures both from frac. A and B were separated on silica-gel columns using hexane, followed by a gradient of CH_2Cl_2 and ethyl acetate up to 100%. Fraction A has yielded compounds with the following order; **1** (20 mg), **2** (59 mg), **3** (7 mg), **4** (4 mg). Fraction B has yielded two known alkaloids; 1-methyl-4-methoxy-2-quinolone (25 mg) and evolitrine (13 mg).

3.3.1. 2-(Nonan-8-one)-(1H)-4-quinolone (*1*)

IR ν^{CHCl_3} (cm^{-1}): 2925, 2850, 1710, 1640, 1595, 1560, 1510, 1460, 1420, 1360, 1190, 1160, 1120, 990, 840, 760. UV λ^{MeOH} (log ε) (nm): 332 (3.8), 3.20 (3.8), 236 (4.2), 216 (4.5). ^{1}H- and ^{13}C-NMR ($CDCl_3$) : Table 1. MS *m/z* (rel. int.) : 285 $[M]^+$ (14), 270 $[M\text{-}Me]^+$ (8), 242 $[M\text{-}COMe]^+$ (47), 228 $[242\text{-}CH_2)^+$ (49), 214 $[228\text{-}CH_2]^+$ (20), 200 $[214\text{-}CH_2]^+$ (11), 186 $[200\text{-}CH_2]^+$ (36), 172 $[186\text{-}CH_2]^+$ (78), 159 $[M\text{-}C_8H_{14}O]^+$ (100), 130 (37), 77 (7). HR-MS *m/z* : 285.1832, calc. for $C_{18}H_{23}NO_2$ 285.1829.

3.3.2. 2-(Nonan-8-one) 4-methoxy-quinoline (*2*)

IR ν^{CHCl_3} (cm^{-1}) : 2930, 2850, 1705, 1595, 1565, 1510, 1450, 1430, 1370, 1190, 1150, 1140, 1000, 980, 840, 760. UV λ^{MeOH} (log ε) (nm): 312 (sh), 314 (2.8), 300 (2.9), 228 (4.5). ^{1}H- and ^{13}C-NMR ($CDCl_3$) : Table 1. MS *m/z* (rel. int.) 299 $[M]^+$ (40), 284 $[M\text{-}Me]^+$ (14), 256 $[284\text{-}CO]^+$ (58), 242 $[256\text{-}CH_2]^+$ (66), 228 $[242\text{-}CH_2]^+$ (25), 214 $[228\text{-}CH_2]^+$ (47), 200 $[214\text{-}CH_2]^+$ (74), 186 $[200\text{-}CH_2]^+$ (89), 173 $[M\text{-}C_8H_{14}O]^+$ (100), 149 (47), 130 (65), 115 (18), 102 (15), 83 (8), 71 (17). HR-MS *m/z* : 299.1978 $[M]^+$, calc. for $C_{19}H_{25}NO_2$ 299.1985.

3.3.3. 2-(Nonan-8-one)-N-methyl-4-quinolone (*3*)

IR ν^{CHCl_3} (cm^{-1}): 2930, 2850, 1712, 1645, 1590, 1560, 1510, 1460, 1420, 1345, 1185, 1165, 1120, 995, 850, 760. UV λ^{MeOH} (log ε) (nm): 332 (3.8), 320 (3.8), 235 (4.5), 220 (4.2). ^{1}H-NMR given in the text. MS *m/z* (rel. int.): 299 $[M]^+$ (75), 284 $[M\text{-}Me]^+$ (20), 256 $[M\text{-}COMe]^+$ (65), 242 $[256\text{-}CH_2]^+$ (60), 242 $[256\text{-}CH_2]^+$ (64), 228 $[242\text{-}CH_2]^+$ (25), 214 $[228\text{-}CH_2]^+$ (8), 200 $[214\text{-}CH_2]^+$ (23), 186 $[200\text{-}CH_2]^+$ (87), 173 $[M\text{-}C_8H_{14}O]^+$ (100), 160 (44), 144 (75), 130 (47), 105 (20), 91 (10), 77 (20). HR-MS *m/z* : 299.1976, calc. for $C_{19}H_{25}NO_2$ 299.1985.

3.3.4. 2-(Decan-9-one)-N-methyl-4-quinolone (*4*)

IR ν^{CHCl_3} (cm^{-1}): 2930, 2860, 1710, 1640, 1590, 1565, 1510, 1465, 1420, 1350, 1190, 1165, 1120, 990. UV λ^{MeOH} (log ε) (nm): 330 (3.7), 320 (3.8) 236 (4.5), 215 (4.1). ^{1}H-NMR given in the text. MS *m/z* (rel. int.): 313 $[M]^+$ (42), 298 $[M\text{-}Me]^+$ (12), 285 $[M\text{-}CO]^+$ (70), 270 $[M\text{-}COMe]^+$ (38), 256 $[270\text{-}CH_2]^+$ (38), 242 $[256\text{-}CH_2]^+$ (36), 228 $[242\text{-}CH_2]^+$ (38), 214 $[228\text{-}CH_2]^+$ (13), 200 $[214\text{-}CH_2]^+$ (50), 186 $[200\text{-}CH_2]^+$ (93), 173 $[M\text{-}C_9H_{14}O]^+$ (100), 160 (42), 144 (68), 130 (40), 105 (20), 77 (17). HR-MS *m/z* : 313.2136 calc. for $C_{20}H_{27}NO_2$ 313.2142.

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