Five New Alkaloids from the Leaves of *Remijia peruviana*

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Three new indolylquinuclidine-type alkaloids, remijinine (**1**), epiremijinine (**2**), and 5-acetyl-apocinchonamine (**3**), and two new cinchonine-derived alkaloids, *N*-acetyl-deoxycinchonicinol (**4**) and *N*-acetyl-cinchonicinol (**5**), as well as the known alkaloids quinamine, conquinamine, cinchonine, and quinidine were isolated from the leaves of *Remijia peruviana*. The structures of the new alkaloids were elucidated on the basis of spectroscopic analysis, including homonuclear and heteronuclear correlation NMR experiments (COSY, ROESY, HMQC, and HMBC). The relative configuration at C-7 for remijinine (**1**) and, in consequence, for epiremijinine (**2**) was established by X-ray crystal structure analysis of the former.

Malaria is a disease that affects nearly 40% of the world's population, causing 1−2 million deaths each year.[1] Despite an international campaign in the mid-20th century to control and eliminate malaria,[2] the incidence of infection continues to increase at a significant rate.[3] A major factor contributing to this increase is the growing spread of resistance to standard antimalarial drug regimens.[4] Hence, with the problem of resistance on one hand and multiple side effects on the other, it became inevitable to look for an alternative drug that would cure the deadly disease.

The leaves of *Remijia* species are used traditionally by the Amazonian population for the treatment of symptoms related to malaria. The present paper describes the isolation and structure elucidation of five new alkaloids and four previously identified compounds from leaves of *Remijia peruviana*.

Results and Discussion

The new alkaloid remijinine (**1**) was obtained as white prisms, crystallized from MeOH−EtOAc, 2:1, $[\alpha]^{25}_{D}$ −21.9° (*c* 0.57, CH_3OH). The molecular formula $C_{19}H_{24}N_2O_2$ was derived from HREIMS (M^+ 312.1825, calcd 312.1837). The UV spectra showed absorption maxima at 207.2, 250.7, and 282.1 nm (log ϵ 4.6, 3.97, and 3.57, respectively), values that are suggestive of oxindole chromophores.[5] The IR spectrum revealed the presence of hydroxyl groups at 3355 cm^{-1}, a γ-lactam at 1685 cm^{-1}, and aromatic rings at 1619 and 1472 cm^{-1}.

The ^1H NMR spectrum ($CDCl_3$, 400 MHz) of **1** (Table 1) suggested an indolylquinuclidine-type alkaloid with a β-hydroxyethyl side chain. The assignments were accomplished by a combination of COSY, HSQC, and HMBC experiments. The proton assignment for the quinuclidine ring was in agreement with previous studies.[6,7] The configuration of C-3 was determined on the basis of the interactions observed in the ROESY experiment between the H-3ex proton and H-21cis, H-14ex, and H-19. The position, intensity, and appearance of the ^1H NMR signals for the indolyl part of **1** are in total agreement with those of the aromatic protons of a 3,3-disubstituted indolin-2-one.[8,9] Two sets of mutually coupled methylene protons at δ 3.69 and 3.61 (HSQC, 58.0 t) and at δ 2.22 and 1.94 (HSQC, 39.4 t) indicated the presence of a β-hydroxyethyl side chain. The HMBC spectrum (Table 1) was used in order to unambiguously interconnect the above-determined three moieties. It showed three-bond connectivities between the one proton triplet at δ 3.19, H-3 of the quinuclidine ring, with carbon resonances at δ_C 180.8 and 129.3 s, C-2 and C-8, respectively, of the indolinone moiety, and with the methylene carbon at δ_C 39.4 t, C-6 of the β-hydroxyethyl side chain. A three-bond correlation was also noted between the nonequivalent C-6 methylene protons and the quaternary carbons, C-2 and C-8, and with the methylene carbon at δ_C 62.9 d, C-3. The two-bond connectivities between C-7 at δ_C 56.3 s with H-3 and the methylene protons at C-6 unambiguously confirmed that the quinuclidine ring and the side chain moiety are linked at the C-7 position.

The remaining details of the molecular structure were determined by single-crystal X-ray diffraction. The structure was solved by direct methods using SIR97.[10] Refinement was performed with SHELXL-93[11] using full-matrix least squares with anisotropic thermal parameters for all non-H atoms. The C-18 and C-19 are disordered between two positions. Some of the hydrogen atoms were found in a difference synthesis map and refined using a riding model, while the remainder were placed at idealized positions and added as a fixed isotropic contribution. The refinement converged at $R_1 = 5.37\%$ and $wR_2 = 14.43\%$, with a goodness of fit of 1.09 for 2198 reflections with $F_o > 4\sigma(F_o)$ and 237 parameters. The largest peak on the final difference map was 0.34 e/Å^3. Figure 1 shows a computer-generated perspective[12] of the final X-ray model of **1**, for which we propose the trivial name remijinine.

Compound **2** was a noncrystalline solid. HRMS gave the molecular formula $C_{19}H_{24}N_2O_2$. The IR and UV spectra were similar to those of **1** [IR (NaCl): 3350 (OH), 1707, γ-lactam, and 1619, 1471 aromatic rings; UV (EtOH): 206 (log ϵ 4.05), 250.8 (log ϵ 3.14), and 287.2 (log ϵ 2.85)].

The ^1H NMR spectrum was also similar to that of **1**, but showed slightly different chemical shifts for H-3, H-5a,b, H-9, H-14en, H-17en, and H-17ex protons (Table 1). The relative configuration at C-3 was determined by a ROESY experiment, which showed a series of bidirectional ROE interactions between the H-3ex proton and H-14ex, H-21c, and H-19. Hence, the relative configuration of C-3 suggested by these connectivities is the same as that for compound **1**. Concerning the C-7 configuration, the splitting of the signals in the ^1H and ^{13}C NMR spectra in the

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Table 1. ^{1}H NMR Data[a] for Compounds **1**−**3** and HMBC Data for Compounds **1** and **2**

	1[b]	**2**[b]	**3**[c]	$HMBC_{H\rightarrow C}$ for **1** and **2**
NH	7.82 s	7.96 s	9.14 s	
H-3ex	3.19 t (7.8)	3.32 t (7.8)		C-2, C-6, C-7, C-8, C-14, C-17, C-21
H-5a	3.69 ddd (12.6, 9.2, 3.6)	3.58 dd (6.0, 5.5)	4.29 d (7.7)	C-6, C-7
H-5b	3.61 dt (12.6, 4.8)	3.56 dd (6.0, 5.5)	4.27 d (7.7)	C-6, C-7
H-6a	2.22 ddd (14.6, 9.2, 4.8)	2.16 ddd (14.5, 5.5, 5.5)	3.28 d (9.0)	C-2, C-3, C-5, C-7, C-8
H-6b	1.94 ddd (14.6, 4.8, 3.6)	2.04 ddd (14.5, 6.0, 6.0)	3.25 d (9.0)	C-2, C-3, C-5, C-7, C-8
H-9	7.64 d (7.5)	7.33 d (7.5)	7.58 brd (7.9)	C-7, C-10, C-11, C-12, C-13
H-10	7.06 td (7.6, 0.7	7.03 td (7.5, 0.6)	7.09 td (7.0, 0.7)	C-8, C-9, C-12, C-13
H-11	7.25 td (7.4, 1.0)	7.23 td (7.7, 0.8)	7.15 td (7.0, 0.9)	C-9, C-13
H-12	6.90 d (7.8)	6.86 d (7.7)	7.32 d (8.1)	C-8, C-9
H-14ex	1.84 m	1.87 m	6.88 d (6.9)	C-3, C-7, C-16, C-20
H-14en	1.08 dd (11.4, 10.2)	1.44 dd (11.0, 10.0)		C-3, C-7, C-16, C-20
H-15	1.76 m	1.79 brs	2.75 ddd (6.9, 5.4, 2.8)	C-3, C-14
H-16ex	1.36 m	1.33 m	1.62 dddd (12.0, 11.0, 4.5, 3.5)	C-14, C-15, C-20
H-16en	1.36 m	1.37 m	1.79 dddd (11.0, 10.0, 4.8, 2.5)	C-14, C-15, C-20
H-17ex	2.65 m	2.39 ddd (13.8, 10.7, 5.0)	2.65 dddd (13.0, 12.0, 9.0, 4.5)	C-3, C-16, C-21
H-17en	3.16 m	2.58 m	2.99 ddd (13.1, 9.0, 5.0)	C-3, C-21
H-18 t	5.05 d (17.1)	5.04 d (17.1)	4.97 d (17.1)	C-15, C-19, C-20, C-21
H-18 c	5.04 d (11.9)	5.01 dd (10.3, 1.1)	4.89 dd (10.1, 1.4)	C-15, C-19, C-20
H-19	5.96 ddd (17.5, 10.0, 7.6)	5.88 ddd (17.4, 10.3, 7.4)	5.62 ddd (17.1, 10.1, 8.4)	C-15, C-20, C-21
H-20	2.29 m	2.24 m	2.60 brd (14.6, 7.2)	C-14, C-18, C-19
H-21t	3.06 dd (13.7, 9.9)	3.01 dd (13.7, 10.2)	3.25 dd (13.9, 9.0)	C-3, C-17, C-19
H-21c	2.88 ddd (13.6, 2.9, 2.9)	2.82 ddd (13.6, 2.9, 2.9)	2.44 ddd (13.0, 5.3, 2.5)	C-3, C-17, C-19
Ac			2.05 s	

[a] Assignments are based on COSY and HMQC experiments. Chemical shifts are in ppm relative to TMS. Coupling constants in parentheses are in Hz. [b] 400 MHz, $CDCl_3$. [c] 500 MHz, $CDCl_3$.

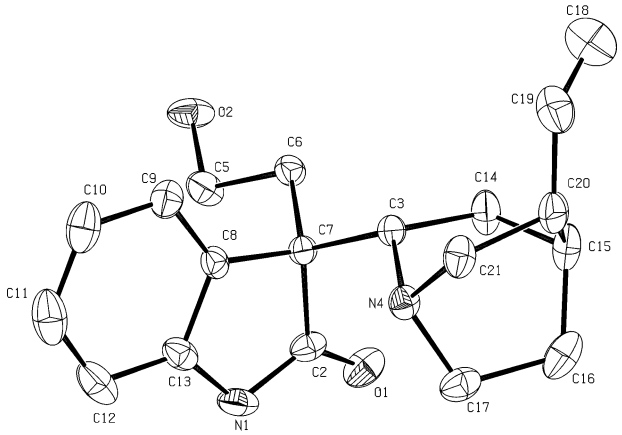


Figure 1. ORTEP drawing of **1**.

environment of the asymmetric center C-7 suggested that it is the opposite of that in **1**.

The two alkaloids **1** and **2** differ in other properties such as their melting point (214−216 °C vs amorphous), specific rotation (−21.9° vs +41.6°), solubility in chloroform, and chromatographic mobility on TLC. This, together with the results of the X-ray analysis for **1**, leads us to conclude that alkaloid **2** is an epimer of remijinine, and we propose the name epiremijinine for this new alkaloid.

Another new alkaloid isolated from the leaves of *R. peruviana* was 5-acetylapocinchonamine (**3**). HRMS gave the molecular formula $C_{21}H_{24}N_2O_2$ (M^+ 336.1826, calcd 336.1838). The IR spectrum showed bands characteristic of an ester group at 1731 cm^{-1} and aromatic rings at 1620 and 1454 cm^{-1}. The UV absorptions at 206 nm (log ϵ 4.26) and 302 nm (log ϵ 3.8) suggested the presence of an indole chromophore.

Comparison of the ^{1}H and ^{13}C NMR spectra of compound **3** (Table 1) with those of **3a** from *Isertia haenkeana*[13] showed a close relationship between both alkaloids. In the case of **3**, the molecular formula and the NMR spectrum showed that the C-5 hydroxyl group was acetylated and the ethyl side chain present in **3a** on the quinuclidine ring was replaced by a vinyl group. The presence of the acetyl group at C-5 was suggested by the downfield shift of the methylene protons at δ_H (4.29 and 4.27 each doublet, J = 7.7 Hz) and corroborated by the long-range correlation observed in the HMBC between the protons attached to C-5 and the carbonyl carbon of the acetyl group. The presence of the vinyl group in 5-acetylapocinchonamine (**3**) was supported by the ^{1}H NMR signals at δ_H 5.62, 4.97, and 4.89.

Compound **4** was a white amorphous powder, $[\alpha]^{25}_D$ +84.0° (*c* 0.79, EtOH). HRMS gave the molecular formula $C_{21}H_{26}N_2O$. The IR showed the presence of an *N*,*N*-disubstituted amide group at 1620 cm^{-1}. The UV spectrum showed absorptions at 205 nm (log ϵ 4.8), 224 nm (log ϵ 4.82), 282 nm (log ϵ 3.96), 300 nm (log ϵ 3.82), and 316 nm (log ϵ 3.7), suggesting the presence of a quinoline ring moiety.[14] The ^{13}C NMR spectra (100 MHz, $CDCl_3$) (Table 3) showed the signals of a methyl amide group, three methylene groups, a *cis*-4-alkyl-3-ethenylpiperidine,[15] and a 4-substituted quinoline moiety.[16]

The ^{1}H NMR spectra (400 MHz, $CDCl_3$) of the *N*-acetyl derivative at room temperature showed that **4** existed in two rotational or geometric isomers in equilibrium. This is possible for amides since they are known to exhibit restricted or slow rotation about the N−CO bond; that is, the compounds have their N−C bond with a partial double-bond character and the resulting spectra are those of two *E*/*Z* isomers. The temperature dependence of these effects was determined. For example, each of the pairs of resonance signals from the *E*/*Z* isomers of compound **4** broadened and then formed a single set of resonance signals as the temperature increased to 323 K (pyridine-d_5).

The basis for the assignment of the configuration of the two isomers is the difference in the chemical shifts of the H-17β and H-21β, in the *E* and *Z* isomers, due to the deshielding by the carbonyl amide group, cis to H-17β and H-21β in the *E* and *Z* form, respectively. The ^{13}C NMR (Table 3) also exhibits significant chemical shift differences for C-17 and C-21 in the two isomers.

Table 2. ^{1}H NMR and HMBC Data[a] for Compounds **4** and **5**

	4[b]	**5**[c]	$HMBC_{H\rightarrow C}$ for **4** and **5**
H-2a	3.04 brd (7.5)	5.42 dd (7.9, 3.9)	C-3, C-6, C-7, C-8, C-14
H-2b	3.01 d (7.5)		
H-3a	1.77 m	1.88 m	C-2, C-7, C-15
H-3b	1.77 m	1.83 m	
H-5	8.79 d (4.4)	8.83 d (4.5)	C-6, C-7
H-6	7.21 d (4.4)	7.52 d (4.3)	C-2, C-5, C-8
H-9	8.00 d (8.3)	7.97 d (8.8)	C-7, C-8, C-11, C-13
H-10	7.55 t (8.2)	7.53 m	C-8, C-9, C-12
H-11	7.70 d (8.5)	7.69 d (7.8)	C-9, C-10, C-13
H-12	8.11 d (8.4)	8.10 d (8.2)	C-8, C-10, C-13
H-14a	1.32 m	1.46 m	C-2, C-3, C-15, C20
H-14b	1.32 m	1.30 m	
H-15α	1.67 m	1.59 m	C-16, C-17, C-19, C-20
H-16α	1.52 ddd (13.5, 2.8, 2.8)	1.43 m	C-15, C-17
H-16*β*	1.42 m	1.32 m	
H-17α	2.59 ddd (13.2, 13.0, 3.4)	2.51 ddd (13.3, 13.0, 3.4)	C-15, C-16, C-21, CO
	3. 08 m	*3.01 ddd (13.0,12.8, 3.4)*	
H-17*β*	4.60 ddd (13.2, 5.6, 2.4)	4.53 brdd (13.2, 2.0)	C-15, C-16, CO
	3.75 brd (14.7)	*3.71 brd (13.3)*	
H-18 c	5.11 d (10.0)	5.04 d (10.0)	C-19, C-20
H-18 t	5.09 d (17.0)	4.98 d (17.4)	
H-19	5.82 ddd (17.0, 10.0, 10.0)	5.72 ddd (17.2, 10.1, 7.8)	C-15, C-20, C-21
H-20α	2.43 m	2.28 m	C-18
H-21α	3.21 dd (13.3, 2.5)	3.15 dd (13.2, 3.2)	C-15, C-17, C-19, C-20, CO
	2.84 dd (13.1, 2.9)	*2.75 dd (13.2, 3.2)*	
H-21*β*	3.70 ddd (13.3, 2.4, 2.4)	3.64 ddd (13.4, 4.6, 2.8)	C-15, C-17, C-19, C-20, CO
	4.42 ddd (13.2, 3.1, 1.8)	*4.39 brd (13.9)*	
N-Ac	2.03 s	1.98 s	CO
	2.08 s	*2.04 s*	

[a] Assignments are based on COSY and HMQC experiments. Chemical shifts are in ppm relative to TMS. Coupling constants in parentheses are in Hz. Values in *italics* are for the minor conformer. [b] 400 MHz, $CDCl_3$, 299.0 K. [c] 500 MHz, $CDCl_3$, 299.0 K.

Table 3. ^{13}C NMR (δ, $CDCl_3$) Data[a] of Compounds **1**−**5**

C	**1**	**2**	**3**	**4**	**5**
C-2	180.8 s	181.4s	143.3s	32.3 t	70.1 d
C-3	62.9 d	62.2	129.2s	27.1 t	35.4 t
C-5	58.0 t	58.2 t	62.9 t	150.1d	150.3 d
C-6	39.4 t	37.9 t	23.8 t	120.7 d	117.9 d
C-7	56.3 s	56.9 s	106.1 s	148.3 s	150.6 s
C-8	129.3 s	131.4s	129.9s	127.5 s	125.4 s
C-9	126.8 d	123.7 d	117.6 d	123.4 d	122.9 d
C-10	122.1 d	122.3 d	118.7 d	126.3 d	126.5 d
C-11	128.3 d	128.3 d	121.3 d	129.0 d	129.0 d
C-12	109.7 d	109.9 d	110.1 d	130.2 d	130.3 s
C-13	141.2 s	140.8 s	133.2 s	148.3 s	148.2 s
C-14	23.2 t	24.2 t	126.5 d	33.3 t	29.4 t
C-15	27.8 d	28.0 d	32.8 d	38.2 d	38.8 d
C-16	27.3 t	27.4 t	28.3 t	27.5 t	27.4 t
C-17	42.9 t	42.8 t	46.9 t	41.8 t	41.8 t
				(46.4 t)	(46.4 t)
C-18	114.8 t	114.6 t	110.1 t	117.8 t	117.4 t
C-19	141.7 d	141.8 d	141.9 d	135.2 d	134.9 d
C-20	39.9 d	39.5 d	45.2 d	43.3 d	43.3 d
C-21	57.8 t	57.8 t	54.9 t	52.3 t	52.2 t
				(46.0 t)	(46.0 t)
C═O			170.4 s	169.3 s	169.4 s
CH_3			20.3 q	21.4 q	21.4 q

[a] Data are based on DEPT, HMQC, and HMBC experiments. Values in parentheses correspond to the minor isomer.

The ^{13}C NMR chemical shifts of the two forms of compound **4** and the connectivities between protons and carbons were established by HSQC and HMBC NMR experiments (Table 2). The ROESY spectrum of **4** showed, among other, interactions between the methyl singlet at δ 2.03 (N-COMe) and the methylene protons at δ 3.21 and 3.70 (H-21α,*β*) of the major isomer. ROESY cross-peaks were also observed between the methyl singlet at δ 2.08 (N-COMe) of the minor isomer and the methylene proton at 3.75 (H-17*β*). The *Z*/*E* ratio was 1:2 in chloroform at 299.0 K, observable from the acetyl protons at δ 2.08 for the *Z* isomer and 2.03 for the *E* isomer.

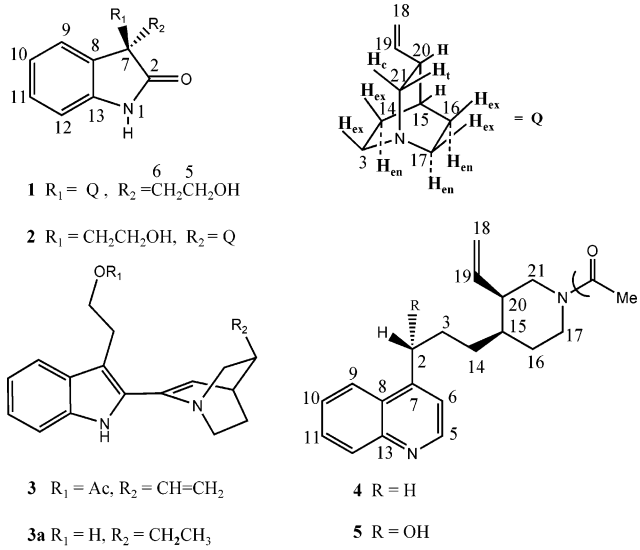
Finally, we dealt with an *N*-acetyl derivative, $C_{21}H_{26}N_2O_2$ (**5**), obtained in a very small amount (less than 1 mg), whose ^{1}H NMR spectrum in chloroform-*d* at room temperature (Table 2) duplicates that of **4**, except for the appearance in **5** of a new signal at δ 5.42 (1 H, dd, J = 7.9 and 3.9 Hz) and HSQC (δ 70.1 d) assignable to a hydrogen geminal to the secondary hydroxyl group. The fragmentation patterns observed in the mass spectrum of **5** at *m*/*z* 159 and 130 suggested a quinuclidine derivative bearing a hydroxyl group at C-2.[17] These spectroscopic data indicated that **5** is *N*-acetylcinchonicinol or its C-2 epimer.

Although paucity of material prevented determination of absolute configuration at C-2, on the basis of the biogenetic pathway it is likely to be the same as that of the parent alcohol, cinchonine, also isolated from the leaves of *R. peruviana*.

Experimental Section

General Experimental Procedures. Melting points were measured on a Reichert Thermovar apparatus and are uncorrected. IR spectra were measured with a Bruker-IFS-55 spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter, 1 dm cell. EIMS and exact mass measurements: Micromass Autospec spectrometer at 70 eV. NMR spectra: Bruker AMX-400 or Bruker AMX-500 spectrometers; $CDCl_3$; δ values in parts per million relative to internal TMS; J values in Hz. Al_2O_3 Merck (neutral, 200−300 mesh) and Schleicher and Schuell 394 732 was used for column chromatography (CC) and TLC, respectively. Sephadex LH-20, Pharmacia. Spots on chromatograms were detected with Dragendorff's reagent.

Plant Material. Leaves of *Remijia peruviana* Standley (Rubiaceae) were collected in November 1998, in Puerto Almendras, Iquitos Province, Peru, and identified by Professor Juan Ruiz Macedo, Faculty of Forest Engineering, Universidad Nacional de la Amazonía Peruana, and a voucher specimen (No. 5402 J. Ruiz) has been deposited in the Herbarium Amazonense of that University.



1 R_1 = Q, R_2 = CH_2CH_2OH

2 R_1 = CH_2CH_2OH, R_2 = Q

3 R_1 = Ac, R_2 = $CH{=}CH_2$

3a R_1 = H, R_2 = CH_2CH_3

4 R = H

5 R = OH

The numbering system shown in **1** and **4** is biogenetically based[20]

Extraction and Isolation. Air-dried and powdered leaves of *R. peruviana* (3.3 kg) were macerated in aqueous-citric acid solutions, pH 2 for 48 h at room temperature. The acidic solution obtained after filtration and evaporation of the solvent to a small volume (about 350 mL) was extracted three times with CH_2Cl_2 (150 mL each) to afford fraction A (1.1 g). The acidic aqueous layer was then adjusted to pH 10 with concentrated NaOH and extracted with CH_2Cl_2 (150 mL × 3) to give fraction B (950 mg).

Fraction A was subjected to column chromatography on Al_2O_3 (activity II). The eluting solvent was a gradient of hexane, EtOAc, and MeOH, and 47 fractions (150 mL each) were collected. Fractions 34−37 (150 mg) on rechromatography over Sephadex LH-20 (hexane−MeOH−$CHCl_3$, 1:1:1) afforded 115 mg of *N*-acetyldeoxycinchonicinol (**4**). Fractions 1−33 and 38−47 containing nonalkaloidal residues were not investigated further.

Fraction B was subjected to column chromatography on Al_2O_3 (activity II) and eluted with hexane−EtOAc and MeOH of increasing polarity, and 100 fractions (150 mL each) were collected. On the basis of TLC results the fractions were pooled to give four subfractions: B-1 (52.4 mg), B-2 (13.2 mg), B-3 (116 mg), and B-4 (250 mg).

Rechromatography of B-1 over Al_2O_3 (50 mL fractions of hexane containing increasing amounts of EtOAc) gave in fractions 10−12, quinamine[13] (16 mg). Combined fractions 14−16 (38.5 mg) were rechromatographed on preparative TLC on SiO_2 eluted with cyclohexane−diethylamine (98:2). Two bands were cut. The upper band gave conquinamine[13] (10.2 mg) and the lower, 5-acetylapocinchonamine (**3**) (8.2 mg). Fraction B-2 (13.2 mg) afforded after purification over preparative TLC on SiO_2 (cyclohexane−diethylamine, 3:1) 6 mg of epiremijinine (**2**). Chromatography of fraction B-3 on alumina, using gradient elution with hexane−EtOAc, followed by further purification over Sephadex LH-20 (hexane−MeOH−$CHCl_3$, 2:1:1) when necessary, allowed the isolation, in order of increasing polarity, of *N*-acetylcinchonicinol (**5**) (0.9 mg), quinidine[6] (5 mg), and cinchonine[6] (43 mg). Trituration of fraction B-4 with MeOH−EtOAc produced solid material, which was recrystallized from MeOH−EtOAc (2:1) to give 136 mg of remijinine (**1**). Known alkaloids were identified by comparison of mp and spectral data (IR, MS, ^{1}H and ^{13} NMR) with literature values

Remijinine (1): prisms, mp 214−216 °C (crystallized from MeOH−EtOAc, 2:1); $[\alpha]_D^{25}$ −21.9° (*c* 0.57, CH_3OH); UV (EtOH) λ max, log(ϵ) 207.2 (4.6), 250.7 (3.97), 282.1 (3.57) nm; IR ν_{max}^{NaCl} 3355, 3131.5, 2932, 1685, 1618, 1472, 1382, 1265.7, 1221.5, 1190.8, 1047, 914.9, 818.8, 756.2, 662.7 cm^{-1}; ^{1}H, ^{13}C NMR (Tables 1 and 3); EIMS *m*/*z* 312 $[M]^+$ (0.4), 297 $[M - Me]^+$(0.3), 283 $[M - CHO]^+$ (0.3), 281 $[M - CH_2OH]^+$ (1.2), 268 $[M - CH_2CH_2OH]^+$ (36), 177 (5), 146 (10), 136 (100); HREIMS *m*/*z* 312.1825 (calcd for $C_{19}H_{24}N_2O_2$, 312.1837).

Epiremijinine (2): amorphous; $[\alpha]_D^{25}$ +41.6° (*c* 0.13, MeOH); UV (EtOH) λ max, log(ϵ) 206 (4.05), 250.8 (3.14), 287.2 (2.85) nm; IR ν_{max}^{NaCl} 3350, 3194.9, 2918, 1701, 1619, 1470, 1346 4, 1216, 1052, 913, 753 cm^{-1}; ^{1}H, ^{13}C NMR (Tables 1 and 3); EIMS *m*/*z* 312 $[M]^+$ (0.3), 281 $[M - CH_2OH]^+$ (1.7), 268 $[M - CH_2CH_2OH]^+$ (59.6), 177 (3.9), 146 (9.2), 136 (100); HREIMS *m*/*z* 312.1809 (calcd for $C_{19}H_{24}N_2O_2$, 312.1837).

5-Acetylapocinchonamine (3): amorphous; $[\alpha]_D^{25}$ +4.6° (*c* 0.22, EtOH); UV (EtOH) λ max, log(ϵ) 206.8 (4.26), 302.2 (3.8), nm; IR ν_{max}^{NaCl} 3288, 2926, 1731, 1620, 1518, 1454, 1367,1238.9, 1043.6, 754.5, 666.3 cm^{-1}; ^{1}H, ^{13}C NMR (Tables 1 and 3); EIMS *m*/*z* 336 $[M]^+$ (35), 308 (18), 294 (10), 281 (66), 277 (27), 265 (56), 249 (100); HREIMS *m*/*z* 336.1826 (calcd for $C_{21}H_{24}N_2O_2$, 336.1838).

***N*-Acetyldeoxycinchonicinol (4):** amorphous $[\alpha]_D^{25}$ +84.0° (*c* 0.79, EtOH); UV (EtOH) λ max, log(ϵ) 205.8, (4.8), 205 (4.8), 224 (4.8), 282 (3.96), 300 (3.82), 316 (3.7) nm; IR ν_{max}^{NaCl} 3443, 3004, 2929, 1644, 1620, 1591, 1570, 1508, 1453, 1362, 1277.6, 1244.5, 1003, 918 765.5 cm^{-1}; ^{1}H, ^{13}C NMR (Tables 2 and 3); ^{1}H NMR (400 MHz, C_5D_5N, 333 K) δ 8.87 (1H, d, *J* = 4.3 Hz), 8.26 (1H, d, *J* = 8.3 Hz), 8.03 (1H, d, *J* = 8.3 Hz), 7.63 (1H, t, d, *J* = 7.0, 1.3 Hz), 7.50 (1H, t, d, *J* = 8.2, 1.1 Hz), 7.18 (1H, d, *J* = 4.3 Hz), 5.72 (1H, ddd, *J* = 17.3, 9.0, 9.0 Hz), 5.03 (1H, d, *J* = 17.3 Hz), 5.0 (1H, d, 9.0 Hz), 4.59 (1H, m), 3.56 (1 H, m), ∼2.91 (1H, m) 2.92 (2H, t, *J* = 7.7 Hz), 2.21 (1H, br s), 1.96 (3H, s, $NCOCH_3$), 1.64 (2H, m), 1.50 (1H, m), between 1.35 and 1.13 (5H, m); EIMS *m*/*z* 322 $[M]^+$ (45), 279 (33), 224 (7.8), 156 (100), 143 (98), 130 (48); HREIMS *m*/*z* 322.2044 (calcd for $C_{21}H_{26}N_2O$, 322.2045).

***N*-Acetylcinchonicinol (5):** amorphous $[\alpha]_D^{25}$ +111.5° (*c* 0.1, EtOH); UV (EtOH) λ max, log(ϵ) 205.6 (4.68), 224.8 (4.5), 283.6 (3.8), 300 (3.78), 314 (3.7) nm; IR ν_{max}^{NaCl} 3354.4, 2923, 1620, 1508, 1450, 1244.4, 1003, 921, 763.5 cm^{-1}; ^{1}H, ^{13}C NMR (Tables 2 and 3); EIMS *m*/*z* 338 $[M]^+$ (100), 321 $[M - OH]^+$ (16), 320 $[M - H_2O]^+$ (45), 295 (10), 159 (4), 130 (92); HREIMS *m*/*z* 338.1943 (calcd for $C_{21}H_{26}N_2O_2$, 338.1994).

X-ray data for remijinine (1): $C_{19}H_{24}N_2O_2$, mol wt = 312.4, orthorhombic, space group $P2_12_12_1$, a = 7.021(2) Å, b = 13.024(4) Å, c = 18.216(7) Å, V = 1665.7(9) Å^3, Z = 4, D_c = 1.246 g·cm^{-3}, $F(000)$ = 672, μ = (Mo Kα) = 0.08 mm^{-1}. A single crystal of approximate dimensions 0.2 × 0.3 × 0.4 mm was used for all X-ray measurements. The intensity data of all unique reflections within the θ range 2.7−28.6° were collected at 273 K in an Enraf-Nonius Kappa CCD diffractometer, using graphite-monochromated Mo Kα (λ = 0.71070 Å) radiation. A total of 2326 unique reflections were recorded, of which 2187 (94.4%) with $F_o > 4\sigma(F_o)$ were taken into account for structure solution and refinements. Data reduction and cell parameter refinement were carried out with the programs COLLECT[18] and DENZO.[19] Crystallographic data of **1**, including atomic coordinates, have been deposited with the Cambridge Crystallographic Data Centre (deposit number 241589). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: 44-(0)1223-306033 or e-mail: deposit@ccdc.cam.ac.uk].

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Supporting Information Available: Crystallographic data for **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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