Coriacenins: A New Class of Long Alkyl Chain Amino Alcohols from the Mediterranean Sponge *Clathrina coriacea*

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The Mediterranean sponge *Clathrina coriacea* contains a series of long chain amino alcohols, named coriacenins (**2**−**6**), belonging to a new class of alkaloids. The structures of the novel compounds were elucidated by studying, with a combination of spectral and chemical methods, their peracetyl derivatives (**2a**−**6a**). Coriacenins are characterized by a *bis*(1,3-diamino-2-propanol) moiety and a linear alkyl chain varying both by length and by degree of unsaturation. The biosynthetic pathway leading to coriacenins seems to be unprecedented. It should, however, occur through condensation of an acetogenin with an uncommon amino acid.

Long chain amino alcohol compounds have been isolated from marine organisms, for example, tunicates[1,2] and porifera.[3−5] The structures of these molecules, often showing significant biological activity, are generally related to the amphiphilic sphingosine. 2-Amino-3-hydroxy hydrocarbons,[3−5] such as leucettamol A (**1**, Chart 1),[5] were isolated by bioassay-guided screening from sponges of the order Demospongiae. Apparently, the biosynthesis of leucettamol-like metabolites differs from that of sphingoid bases, because it should involve the amino acid alanine,[4] and not serine, in the coupling with fatty acids.

In our study of secondary metabolism of invertebrates from the Mediterranean Sea, we found that the polar extract of the calcarea sponge *Clathrina coriacea* (Montayer, 1812) contained a new class of lipid (**2**−**6**), containing a novel 1,3-diamino-2-propanol moiety. These new compounds, named coriacenins, appear to be related neither to other amino alcohols, such as sphingosine-type compounds,[1−5] nor to widespread polyamines, like spermine or spermidine, nor to other known lipid alkaloids. Here we report the isolation and chemical characterization of the peracetyl derivatives of the coriacenins **2a**−**6a** (Figure 1).

The sponge *C. coriacea* (order Calcinea, family Clathrinidae) was collected along the SE Spanish coasts, frozen, and transferred to Naples. The BuOH−soluble fraction from the acetone extract of the sponge was fractionated by Sephadex chromatography affording a mixture of polar metabolites positive to Dragendorff's reagent. NMR data of this fraction showed characteristics of an unsaturated long alkyl chain bearing many hydroxy and amino groups. After acetylation under mild conditions, three acetyl groups (δ 2.14, 2.05, and 2.01), together with an exchangeable signal at δ 6.79 assigned to a NH proton, were observed in the ^{1}H NMR spectrum of the peracetylated mixture. The poor resolution of spin systems and the presence of many ^{13}C NMR signals with different intensities (134−123 ppm) supported the hypothesis that the mixture contained a series of related products exhibiting different olefinic substitution patterns. Treatment of the mixture with Na_2CO_3/MeOH gave, after silica gel purification, a mixture showing only two acetyl signals (δ 2.13 and 2.01) in the ^{1}H NMR spectrum. The loss of the third acetyl moiety (δ 2.05) matched the upfield shift of a carbinol proton from 4.93 ppm (in the peracetyl fraction) to 3.84 ppm. As the methanolysis conditions are able to cleavage an ester linkage, but not an amide bond, the experiment demonstrated that the structures of coriacenins include two amino groups and one alcohol function.

Further HPLC on reverse phase media gave pure peracetyl derivatives of coriacenin A−C (**2a**−**4a**) and peracetyl coriacenin D (**5a**) in semipure form, together with an unresolved mixture of triacetylated compounds.

Peracetyl coriacenin A (**2a**) was isolated as an optically active oil ($[\alpha]_D = -6.1°$ ($c = 0.24$, $CHCl_3$)). The positive HRFABMS showed a molecular ion at m/z 735.5343 [M + H]$^+$ (required 735.5272), which corresponds to the formula $C_{40}H_{70}N_4O_8$ for the free amide. Apart from the molecular ion at m/z 735 (M + H$^+$, 100), the FAB$^+$ MS spectrum was characterized by two main fragments (m/z 693 and 675), formed from the loss of ketene or acetic acid. The IR spectrum showed typical absorptions for amine (3429 cm^{-1}), ester (1740 cm^{-1}), and amide (1636 and 1650 cm^{-1}) moieties. Besides the resonances of three acetyl groups (δ 2.16, 2.05, and 1.97), the ^{1}H NMR spectrum exhibited a downfield quintet at δ 4.94 (H-3 and H-30) that, after homodecoupling and ^{1}H−^{1}H COSY experiments (Figure 2), showed connectivity with two aminomethylene groups (δ 3.72 and 3.34, H-4 and H-29; δ 3.48 and 3.19, H-2 and H-31) (Figure 2). All these ^{1}H NMR signals were correlated by HMQC to the ^{13}C NMR resonances at δ 70.5 (C-3 and C-30), 45.2 (C-4 and C-29), and 39.0 (C-2 and C-31), respectively. The ^{1}H NMR spectrum also revealed an exchangeable triplet at 6.74 ppm (NH) coupled with the methylene protons at δ 3.48 and 3.19, and a third aminomethylene group (^{1}H NMR δ 3.30, H-6 and H-27; ^{13}C NMR δ 49.5). These data were consistent with the presence of the partial structure **a**.

The ^{1}H NMR data were completed by two vinyl protons at δ 5.52 (H-8 and H-25) and 5.25 (H-9 and H-24) and the spin systems of four allylic (δ 2.32, H-7 and H-26; δ 2.03, H-10 and H-23) methylene protons, together with

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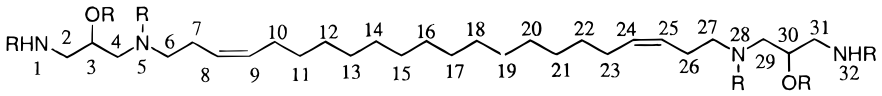
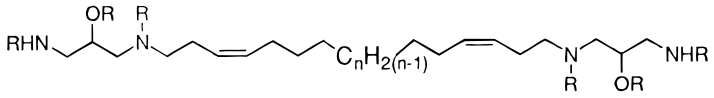
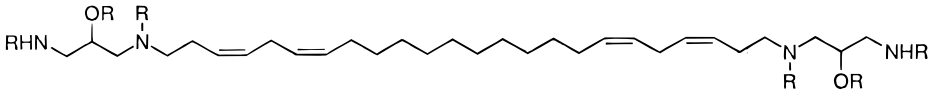
a)



2 R=H
2a R=Ac

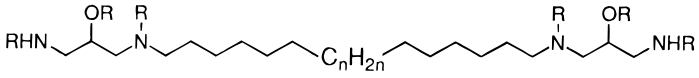


3 n=9, R=H; **3a** n=9, R=Ac
4 n=11, R=H; **4a** n=11, R=Ac
6 n=10, R=H; **6a** n=10, R=Ac



5 R=H
5a R=Ac

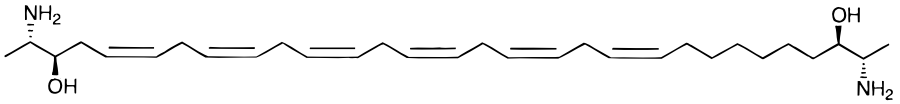
b)



7 n=10, R=Ac
8 n=11, R=Ac
9 n=12, R=Ac

Figure 1. (a) Structures of natural (**2**−**6**) and peracetylated coriacenins A−E (**2a**−**6a**); (b) main homologues (**7**−**9**) obtained by hydrogenation of the crude peracetyl mixture of coriacenins.

Chart 1



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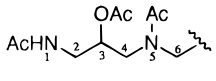
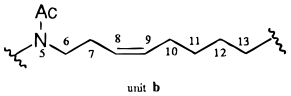
the signal at 1.24 ppm of a linear alkyl chain. Irradiation of the aminomethylene protons (δ 3.30, H-6 and H-27) simplified the signal of the allylic hydrogens at 2.32 (H-7 and H-26) indicating a strong coupling between them (Figure 2). The compound, therefore, revealed an unsaturated long alkyl chain (see partial structure **b**) connected to the nitrogen atom of the terminal 1,3-diamino-2-propanol moiety. No branching of the alkyl chain was indicated by the NMR data. Considering the molecular weight and the absence of a terminal methyl group, the structure of peracetyl coriacenin A was unambiguously determined as **2a**.



unit **a**



unit **b**

The *cis* configuration of the two double bonds was suggested by both the coupling constant (J = 10.5 Hz) between the olefin protons and the upfield ^{13}C NMR resonances at δ 26.5 and 27.4 of C-7 and C26, and C-10 and C-23, respectively. To the best of our knowledge, the structure of coriacenin A is an unprecedented one.

Peracetyl derivatives of coriacenin B (**3a**) and coriacenin C (**4a**) showed a ^{1}H NMR very similar spectrum to that of **2a**. Nevertheless, both the compounds contain one more double bond than coriacenin A. The molecular formula of **3a** ($C_{40}H_{68}N_4O_8$) required nine unsaturations. FAB$^+$ MS showed a molecular ion at m/z 733 (M + H$^+$) and two main peaks of fragmentation at m/z 691 and 673 due to the loss of ketene or acetic acid, as previously described for **2a**. Peracetyl coriacenin C (**4a**) is a higher homologue than **3a**. Its HRFAB spectrum showed a molecular ion peak at 761.5495 (required 761.5485) corresponding to the molecular formula $C_{42}H_{72}N_4O_8$ (nine unsaturations) for the free amide; FABMS revealed a molecular ion at m/z 761 associated with the typical fragments at M − 42 + H$^+$ (m/z 719) and M − 60 + H$^+$ (m/z 701). The nature of the alkyl chains of **3a** and **4a** was assigned by comparison of ^{1}H NMR data with those of peracetyl coriacenin A. Unfortunately, the ^{1}H NMR data of these compounds and the poor fragmentation of FAB spectra did not allow us to establish the position of the third double bond which, therefore, still remains unassigned.

Peracetyl coriacenin D (**5a**) displayed a close similarity to **2a**−**4a**, although the ^{1}H NMR spectrum of this fraction was characteristic in that it showed a bis unconjugated diene, with olefin resonances at δ 5.49 and 5.29 and four bis-allylic protons at δ 2.79 (H-10 and H-25). The

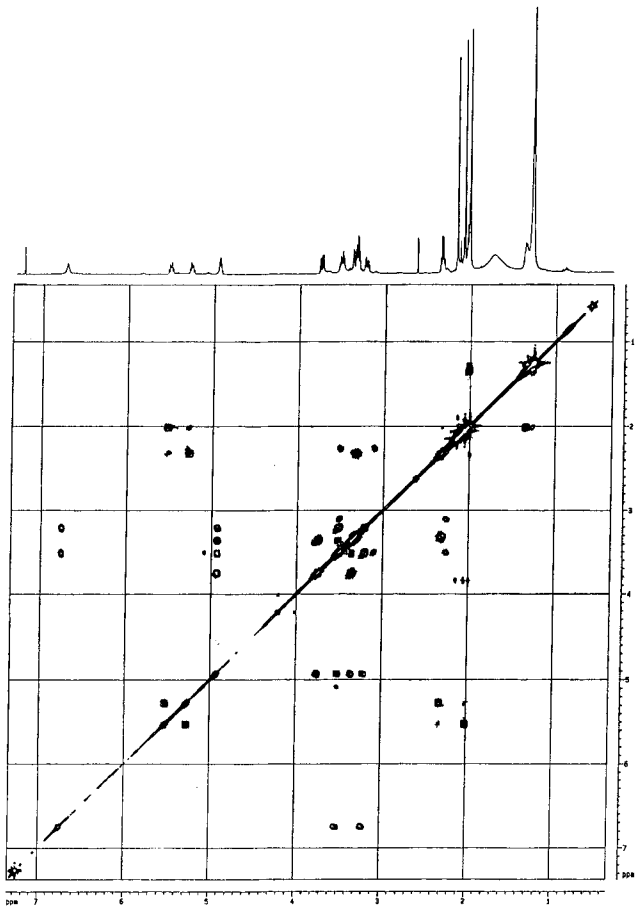


Figure 2. $^1H-^1H$ COSY spectrum of peracetyl coriacenin A (**2a**). Data were measured in $CDCl_3$ on a 500 MHz spectrometer.

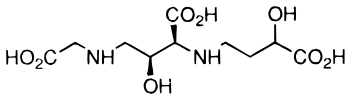
irradiation on allylic protons at δ 2.29 (H-7 and H-28) simplified the signal of the aminomethylene group at 3.34 ppm (H-6 and H-29), suggesting that the ends of the alkyl chain were identical to those observed for **2a**. Although minor components were present, the *cis* stereochemistry for the double bonds was suggested by ^{13}C NMR resonances at δ 26.3 (2C, t) assigned to the carbons of two bis-allyl methylenes.[5] The HRFABMS of the molecular ion peak (*m/z* 759.5341; required 759.5272) revealed a molecular formula of $C_{42}H_{70}N_4O_8$ (10 unsaturations) that, considering the presence of two diamino-2-propanol groups, was consistent with the structure of **5a**. Finally, FAB$^+$MS showed a main pattern characterized by two peaks of fragmentation at *m/z* 717 [(M − 42) + H$^+$] and 699 [(M − 60) + H$^+$] due to the loss of acetic acid and ketene.

To confirm the alkyl chain length of the sponge metabolites, a crude mixture of acetyl derivatives was hydrogenated by H_2/Pd. HPLC of the reduced products achieved separation into three main homologues **7**−**9** with alkyl chain lengths of 22 [*m/z* 739.5635 (required 739.5585) derived from structures **2**, **3**], 23 [*m/z* 753.5798 (required 753.5741)], and 24 [*m/z* 767.5980 (required 767.5989) derived from structures **4**, **5**] carbon atoms (see Table 1). The presence of compounds containing a 23-carbon alkyl chain prompted a deep analysis of the mass spectral data of the complex mixture obtained unresolved by HPLC. The FAB MS ion cluster at *m/z* 747 (M + H$^+$), 705 [(M − 42) + H$^+$], and 687 [(M − 60) + H$^+$] supported the presence, at least, of another component to which the structure **6a** was tentatively assigned.

Table 1. HRFAB and FAB$^+$ MS Spectra of Peracetyl Coriacenins A−E (2a-6a). Spectra were recorded by Using Glycerol as Matrix

	mol form	HRFAB	M + H$^+$	(M − 42) + H$^+$	(M − 60) + H$^+$
2a	$C_{40}H_{71}N_4O_8$	735.5343	735	693	675
3a	$C_{40}H_{69}N_4O_8$	733.5180	733	691	673
4a	$C_{42}H_{73}N_4O_8$	761.5495	761	719	701
5a[a]	$C_{42}H_{71}N_4O_8$	759.5341	759	717	699
6a[a]	$C_{41}H_{71}N_4O_8$		747	705	687
7	$C_{40}H_{75}N_4O_8$	739.5635	739	697	679
8	$C_{41}H_{77}N_4O_8$	753.5798	753	711	693
9	$C_{42}H_{79}N_4O_8$	767.5980	767	725	707

Compounds **2a**−**6a** possess two asymmetric carbon centers. Due to the symmetric nature of the molecules, coriacenins can be chiral, racemic, or meso compounds. Attempts were made to define the absolute stereochemistry of carbinol centers by using Mosher's method[6−8] on the desacetylated mixture, but no results were obtained (see Experimental Section). The stereochemistry nature of coriacenins, therefore, still has to be solved, although the presence of the meso and racemic compounds can be excluded on the basis of the optical acitivity of **2a** and of the hydrogenated compounds **7**−**9** (see Experimental Section).



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Conclusion

Sponges of the genus *Clathrina* are a well-known source of imidazolyl alkaloid clathridine,[9,10] which is absent in *C. coriacea*. The polar extract of *C. coriacea* contains a family of metabolites showing different unsaturated alkyl chains bearing, at both the ends, a polar 1,3-diamino-2-propanol moiety. We have identified four different compounds belonging to a homologous series with an alkyl chain containing either 22 or 24 carbon atoms. Only tentatively, the missing homologue of the series has been identified by analysis of the FAB MS spectrum of an HPLC fraction. These polyunsaturated amino alcohols are the first examples of a new class of natural products. To the best of our knowledge, the closest amino alcohol compounds similar to the coriacenins are the leucettamols[5] (**1**), recently isolated together with clathridine[11] from *Leucetta microraphis*.

Although the structure of coriacenins is similar to that of the leucettamols, the biosynthesis of coriacenins can be hardly similar. In fact, a sphingosine-like biosynthetic pathway, as already proposed for leucettamol analogues,[4] cannot be assumed for the formation of the 1,3-diamino-2-propanol moiety of coriacenins. At the moment two distinct pathways can be advanced: coriacenins could be derived either through the coupling of an acetogenin with an unknown amino acid or by following a biosynthesis

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comparable to that of spermine. It is quite interesting that the first hypothesis should involve an amino acidic structure not previously found, even if a similar feature is present in the skeleton of distichonic acid (**10**), isolated in Nature from *Hordeum vulgare*.[12] The spermine-like biosynthesis should involve first the coupling of an α,ω-diamino long alkyl chain precursor with a propylamine residue, deriving from decarboxylated *S*-adenosylmethionine, and then the hydroxylation of the tetraamine precursor.

The absolute stereochemistry of coriacenins has to be defined, and in order to do this the synthesis of **2a** is in progress.

Experimental Section

Materials. Merck kieselgel 60 (70−230 mesh) was used for silica gel chromatography and precoated kieselgel 60 F254 plates (0.25 mm precoated plates) were used for analytical TLC. NMR spectra were recorded by WM-500 (500 MHz) and AMX 400 (400 MHz) spectrometers. Chemical shifts are reported in ppm referenced to $CHCl_3$ ($\delta = 7.26$ for proton and 77.0 for carbon). Low- and high-resolution FAB spectra were obtained by using glycerol as matrix. IR spectra were recorded in liquid film.

Optical rotations were measured in $CHCl_3$. HPLC was performed on a Sperisorb ODS-2 5 μm (180 × 4 mm i.d.) column. Elution was carried out by using CH_3CN/H_2O (70:30) for natural peracetyl coriacenins and CH_3CN/H_2O (80:20) for hydrogenated derivatives. Solvents for synthesis were dried prior to use.

Extraction and Purification. *C. coriacea* was collected off Tarifa Island (South of Spain) in August and November 1994. The sponge (250 g wet weight), frozen after the collection, was extracted with acetone (250 mL). After removal of organic solvent, the aqueous suspension was diluted with fresh water (200 mL) and extracted three times (3 × 200 mL) with diethyl ether and subsequently with *n*-butanol (3 × 150 mL). The BuOH-soluble fraction was fractionated and evaporated to obtain an oily residue (860 mg) that was resolved by chromatography on Sephadex LH-20 eluting with MeOH. The elution of products was followed by 1 N $CeSO_4-H_2SO_4$ and by Dragendorff's reagent. The positive fractions were combined to give **2**−**6**: yellow oil (140 mg); ^{1}H NMR (CD_3OD) δ 5.62 (m), 5.40 (m), 3.50−2.80 (many overlapped protons), 2.56 (m), 2.15 (m), 1.32 (m, alkyl chain); ^{13}C NMR (CD_3OD) δ 25.6 (t), 26.4 (t), 27.9 (t), 28.0 (t), 30.2 (t), 30.4 (t, alkyl chain), 43.8 (t), 48.0 (q), 51.5 (t), 65.6 (t), 123.0−136.0 (d, many olefinic carbons).

Acetylation of Coriacenin Mixture. The partially purified mixture of **2**−**6** was treated by dry pyridine (4.5 mL) and distilled acetic anhydride (1 mL) at room temperature overnight. After the solvent was removed, the reaction mixture was fractionated on silica gel column by eluting with 95/5 $CHCl_3$:MeOH to yield **2a**−**6a**: yellow oil (76 mg); ^{1}H NMR ($CDCl_3$) δ 6.79 (m), 5.50 (m), 5.30 (m), 4.93 (bt), 3.74 (m), 3.52 (m), 3.32 (m), 3.26 (m), 2.81 (m), 2.31 (m), 2.14 (s), 2.05 (s), 2.01 (s), 1.24 (bs, alkyl chain); ^{13}C NMR ($CDCl_3$) δ 20.8 (q, 21.1 (q), 23.0 (q), 25.4 (t), 26.3 (t), 27.0 (t), 28.7−29.4 (t), 38.9 (t), 45.2 (t), 49.1 (t), 49.3 (t), 70.3 (d), 123.7−133.4 (d), 170.1 (s), 170.4 (s), 171.7 (s).

Purification of Peracetyl Coriacenins A−**D**. Reverse phase (ODS-2 5 μm, 180 × 4; elution with $CH_3CN:H_2O$ 70/30; monitoring by differential refractometer) HPLC purification of the peracetyl mixture (30 mg) achieved separation into **2a** (2.4 mg, 0.66% of BuOH extract), **3a** (0.8 mg), **4a** (1.6 mg), and **5a** (1.1 mg) together with an unresolved mixture of triacetylated compounds.

Peracetyl coriacenin A (2a): yellow oil (2.4 mg); $[\alpha]_D = -6.1°$ ($c = 0.24$, $CHCl_3$); IR (MeOH solution) 3429, 2924, 2584, 1740, 1650, 1636, 1234 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.74 (2H, bt, $J = 6.1$ Hz, NH), 5.52 (2H, bq, $J = 10.5$ and 7.9 Hz, H-8 and H-25), 5.25 (2H, bq, $J = 10.5$ and 7.9 Hz, H-9 and H-24), 4.94 (2H, q, $J = 5.5$ Hz, H-3 and H-30), 3.72 (2H, dd, $J = 14.5$ and 6.5 Hz, H-4a and H-29a), 3.48 (2H, m, H-2a and H-31a), 3.34 (2H, dd, $J = 14.5$ and 6.5 Hz , H-4b and H-29b), 3.30 (4H, m, H-6 and H-27), 3.19 (2H, ddd, $J = 14.5$, 6.1, and 5.2 Hz, H-2b and H-31b), 2.32 (4H, q, $J = 7.4$ Hz, H-7 and H-26), 2.16 (6H, s, C*H*$_3$CO-), 2.05 (6H, s, C*H*$_3$CO-), 2.03 (4H, m, H-10 and H-23), 1.97 (6H, s, C*H*$_3$CO-), 1.36 (4H, m), 1.24 (20H, m); ^{13}C NMR ($CDCl_3$) δ 21.1 (q, *C*H$_3$CO-), 21.4 (q, *C*H$_3$CO-), 23.3 (q, *C*H$_3$-CO-), 26.5 (t, C-7 and C-26), 27.4 (t, C-10 and C-23), 29.3 (t, alkyl chain), 29.5 (t, alkyl chain), 29.7 (t, alkyl chain), 39.0 (t, C-2 and C-31), 45.2 (t, C-4 and C-29), 49.5 (t, C-6 and C-27), 70.5 (d, C-3 and C-30), 123.9 (d, C-8 and C-24), 133.7 (d, C-9 and C-24), 170.1 (s, CH$_3$*C*O-), 170.4 (s, CH$_3$*C*O-), 171.7 (s, CH$_3$*C*O-); HRFABMS obsd m/z 735.5343 (M + H$^+$), $C_{40}H_{70}N_4O_8$ requires 735.5272. For FAB$^+$ MS see Table 1.

Peracetyl coriacenin B (3a): yellow oil (0.8 mg); $[\alpha]_D = -6.3°$ ($c = 0.08$, $CHCl_3$); IR (MeOH solution) 3429, 2924, 1736, 1651, 1636, 1261 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.76 (2H, bt, $J = 6.1$ Hz, NH), 5.52 (2H, bq, $J = 10.5$ and 8.0 Hz , H-8 and H-25), 5.34 (2H, m), 5.25 (2H, m, H-9 and H-24), 4.92 (2H, q, $J = 5.6$ Hz, H-3 and H-30), 3.75 (2H, dd, $J = 14.5$ and 6.5 Hz, H-4a and H-29a), 3.48 (2H, m, H-2a and H-31a), 3.33 (6H, m, H-4b, H-29b, H-6 and H-27), 3.21 (2H, m, H-2b and H-31b), 2.33 (4H, q, $J = 7.4$ Hz, H-7 and H-26), 2.14 (6H, s, C*H*$_3$CO-), 2.05 (6H, s, C*H*$_3$CO-), 2.00 (6H, s, C*H*$_3$CON-), 1.36 (4H, m, H-11 and H-22), 1.24 (20H, m); HRFABMS obsd m/z 733.5180 (M + H$^+$), $C_{40}H_{69}N_4O_8$ requires 733.5115; FAB$^+$ MS, see Table 1.

Peracetyl coriacenin C (4a): yellow oil (1.6 mg); $[\alpha]_D = -6.2°$ ($c = 0.16$, $CHCl_3$); IR (MeOH solution) 3429, 3389, 2924, 2854, 1740, 1650, 1639, 1231 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.76 (2H, bt, $J = 6.1$ Hz, NH), 5.52 (2H, bq, $J = 10.5$ and 8.0 Hz , H-8 and H-27), 5.37 (1H, m), 5.25 (3H, m, H-9 and H-26), 4.91 (2H, q, $J = 5.6$ Hz, H-3 and H-32), 3.77 (2H, dd, $J = 14.5$ and 6.5 Hz, H-4a and H-31a), 3.51 (2H, m, H-2a and H-33a), 3.34 (6H, m, H-4b, H-6 and H-29, H-31b), 3.21 (2H, m, H-2b and H-33b), 2.33 (4H, q, $J = 7.4$ Hz, H-7 and H-28), 2.14 (6H, s, C*H*$_3$CO-), 2.09 (4H, m, H-10 and H-25), 2.05 (6H, s, C*H*$_3$CO-), 2.01 (6H, s, C*H*$_3$CO-), 1.36 (4H, m, H-1 and H-24), 1.24 (24H, m); HRFABMS obsd m/z 761.5495 (M + H$^+$), $C_{42}H_{73}N_4O_8$ requires 761.5428; for FAB$^+$ MS, see Table 1.

Peracetyl coriacenin D (5a): yellow oil (1.1 mg); $[\alpha]_D = -10.0°$ ($c = 0.36$, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.81 (2H, bt, $J = 6.1$ Hz, NH), 5.49 (2H, bq, $J = 10.5$ and 8.0 Hz , H-8 and H-27), 5.29 (6H, m, H-9, H-11, H12, H-23, H-24 and H-26), 4.92 (2H, q, $J = 5.6$ Hz, H-3 and H-32), 3.72 (2H, dd, $J = 14.5$ and 6.5 Hz, H-4a and H-31a), 3.48 (2H, m, H-2a and H-33a), 3.34 (6H, m, H-4b, H-31b, H-6 and H-29), 3.19 (2H, m, H-2b and H-33b), 2.79 (4H, m, H-10 and H-25), 2.29 (4H, m, H-7 and H-28), 2.11 (6H, s, C*H*$_3$CO-), 2.09 (4H, m, H-13 and H-22), 2.02 (6H, s, C*H*$_3$CO-), 1.97 (6H, s, C*H*$_3$CO-), 1.37 (4H, m, H-14 and H-21), 1.24 (12H, m); HRFABMS obsd m/z 759.5341 (M + H$^+$), $C_{42}H_{71}N_4O_8$ requires 759.5272; for FAB$^+$ MS, see Table 1.

Deacetylation of Coriacenins. A mixture of peracetyl derivatives of coriacenins (**2a**−**6a**; 20 mg) was treated with Na_2CO_3 (10 mg) in dry MeOH (3 mL). The reaction was stirred at 40° C overnight; then, the white suspension was neutralized by 6 N HCl, diluted with distilled water (3 mL), and extracted by $CHCl_3$ (5 mL) three times. The organic layer was dried on Na_2SO_4, and filtered through paper, and after removal of the solvent, the residue was purified by column chromatography on silica gel to give the desacetylated mixture (7 mg): ($[\alpha]_D = -21.3°$, $c = 0.26$, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.69 (bt, $J = 6.1$ Hz, NH), 5.51 (bq, $J = 10.5$ and 8.0 Hz), 5.32 (m), 3.84 (m), 3.53 (m), 3.28 (m), 3.11 (m,), 2.81 (m), 2.30 (m), 2.13 (s, C*H*$_3$-CO-), 2.09 (m), 2.01 (s, C*H*$_3$CO-), 1.24 (m).

Perhydrocoriacenins (7−**9).** Hydrogenation of a crude mixture (18 mg) of peracetyl derivatives of coriacenins was carried out under standard conditions by using H_2 (low pressure; about 3 atm) and as catalyst 10% Pd (20 mg) on carbon in CH_2Cl_2 (5 mL) at rt overnight. The reaction was filtered through paper and the filtrate concentrated to remove the organic solvent. The residue was dissolved in MeOH and directly fractionated by reverse phase HPLC (ODS-2 5 μm, 180 × 4 mm i.d.; elution with 90/10 $CH_3CN:H_2O$; monitoring by differential refractometer) to give pure **7**−**9**.

(12) In *Dictionary of Natural Products*, Version 4:2, February 1996, Chapman & Hall Electronic Publishing Division.

Compound 7: straw-yellow oil (2.4 mg); $[\alpha]_D = -8.7°$ (c = 0.24, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.77 (2H, bt, J = 6.1 Hz, NH), 4.93 (2H, q, J = 5.5 Hz, H-3 and H-30), 3.75 (2H, dd, J = 14.5 and 6.5 Hz, H-4a and H-29a), 3.52 (2H, ddd, J = 14.5, 5.7, and 5.5 Hz, H-2a and H-31a), 3.33 (2H, dd, J = 14.5 and 6.5 Hz , H-4b and H-29b), 3.26 (4H, m, H-6 and H-27), 3.17 (2H, ddd, J = 14.5, 5.7, and 5.5 Hz, H-2b and H-31b), 2.13 (6H, s, CH_3CO-), 2.06 (6H, s, CH_3CO-), 2.00 (6H, s, CH_3CO-), 1.30−1.24 (40H, m); HRFABMS obsd m/z 739.5635 ($M + H^+$), $C_{40}H_{75}N_4O_8$ requires 739.5585; for FAB^+ MS, see Table 1.

Compound 8: straw-yellow oil (1.4 mg); $[\alpha]_D = -8.9°$ (c = 0.14, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.77 (2H, bt, J = 6.1 Hz, NH), 4.93 (2H, q, J = 5.5 Hz, H-3 and H-31), 3.75 (2H, dd, J = 14.5 and 6.5 Hz, H-4a and H-30a), 3.53 (2H, ddd, J = 14.5, 6.1 and 5.5 Hz, H-2a and H-32a), 3.33 (2H, dd, J = 14.5 and 6.5 Hz , H-4b and H-30b), 3.26 (4H, m, H-6 and H-28), 3.17 (2H, ddd, J = 14.5, 6.1, and 5.5 Hz, H-2b and H-32b), 2.13 (6H, s, CH_3-CO-), 2.06 (6H, s, CH_3CO-), 2.00 (6H, s, CH_3CO-), 1.30−1.24 (42H, m); HRFABMS obsd m/z 753.5798 ($M + H^+$), $C_{41}H_{77}N_4O_8$ requires 753.5741; for FAB^+ MS, see Table 1.

Compound 9: straw-yellow oil (1.1 mg); $[\alpha]_D = -8.9°$ (c = 0.10, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.81 (2H, bt, J = 6.1 Hz, NH), 4.92 (2H, q, J = 5.5 Hz, H-3 and H-32), 3.75 (2H, dd, J = 14.5 and 6.5 Hz, H-4a and H-31a), 3.53 (2H, ddd, J = 14.5, 6.1, and 5.5 Hz, H-2a and H-33a), 3.33 (2H, dd, J = 14.5 and 6.5 Hz , H-4b and H-31b), 3.26 (4H, m, H-6 and H-29), 3.17 (2H, ddd, J = 14.5, 6.1, and 5.5 Hz, H-2b and H-33b), 2.13 (6H, s, CH_3CO-), 2.06 (6H, s, CH_3CO-), 2.00 (6H, s, CH_3CO-), 1.32−1.24 (44H, m); HRFABMS obsd m/z 767.5980 ($M + H^+$), $C_{42}H_{79}N_4O_8$ requires 733.5989; for FAB^+ MS, see Table 1.

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Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra of the mixture **2a**−**6a** and DEPT and ^1H and ^{13}C NMR of the pure peracetyl coriacenin A (**2a**) together with ^1H NMR spectra of compounds **3a**−**6a**, **7**−**9**, the crude mixture **2**−**6**, and the desacetylated fraction (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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