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Eunicenones A and B: Diterpenoid Cyclohexenones of a Rare Skeletal Class from a New Species of the Caribbean Gorgonian *Eunicea* ‡

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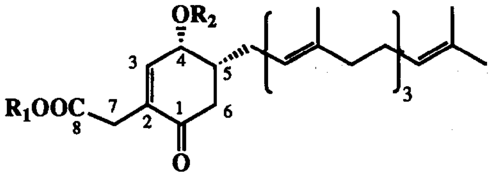
Abstract: Eunicenones A and B (1 and 2), compounds of a mixed biosynthetic origin, have been isolated from a new species of the Caribbean gorgonian genus *Eunicea*. The new compounds are diterpenoid cyclohexenones of a new skeletal class related in part to the linear diterpenoid-substituted quinones and hydroquinones isolated from various plants and animals. The structures of 1 and 2 were determined by spectral and chemical methods, and the absolute stereochemistries of these metabolites were determined by CD methods.

Marine octocorals (Phylum Cnidaria) of the order Gorgonaceae, the sea whips and sea fans, are among the most chemically-prolific of the invertebrate groups.[2,3] Gorgonians of the common Caribbean genus *Eunicea* were among the first marine invertebrates to be chemically investigated.[4] Although common and abundant, the morphological variability in this genus (size, color and overall physical characteristics) resulting in difficulties in making secure species assignments has impeded a comprehensive chemical evaluation of this group. In consultation with a specialist in gorgonian systematics,[5] we have subsequently been able to provide a more thorough evaluation of these animals throughout the Caribbean Sea.[6] Our approach has been to make comprehensive collections in a single site and to examine the chemistry of each individual colony by TLC analyses in two different solvent systems. Using this approach, we were able to combine specimens which possessed significant morphological variations into homogeneous chemotypes which were later examined and confirmed to be single species. As a result, we have been able to show that the natural products chemistry of *Eunicea* species

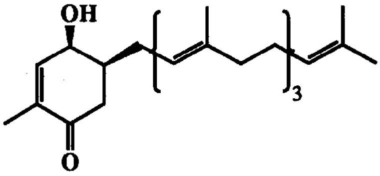
‡ Dedicated to Professor Carl Djerassi on the occasion of his seventieth birthday.

is much more diverse than initially conceived.

As part of this continuing chemical investigation, we encountered a new *Eunicea* species in the Tobago Cays, eastern Caribbean Sea, which is chemically-distinct from all other members of this genus.[7] In this paper we report the isolation of two novel metabolites, eunicenones A and B (**1** and **2**) which possess previously unobserved C_{28} carbon skeletons. Related polyprenylquinones and hydroquinones are widely distributed in both terrestrial and marine plants and animals. In marine habitats, brown algae of the order Fucales and sponges of the order Dictyoceratida are common sources.[3,8] Related metabolites also have been isolated from the ascidian *Aplidium californicum,* [9] the soft coral *Nephthea* sp.[10] and the gorgonian *Plexaura flava.*[11] Recently, Pietra and coworkers reported the isolation of sarcodictyenone (3), a ring-reduced diterpenoid quinone from the Mediterranean stoloniferan *Sarcodictyon roseum.*[12] The structures of the eunicenones are similar to sarcodictyenone, however these metabolites possess oxidized ethyl substituents at C-2 on the cyclohexenone ring. To the best of our knowledge, these are the first examples of diterpenoids with this C_8 component.



	R₁	**R₂**
1	Me	H
2	H	Ac



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Eunicea (CI86-183) specimens were briefly air-dried and stored frozen. The animals were macerated and extracted with dichloromethane, and the condensed extract was fractionated by silica vacuum flash chromatography. Fractions eluted with moderate polarity solvents were subsequently fractionated by silica and C-18 reversed-phase HPLC to yield eunicenones A and B (**1, 2**) as 1.0 and 1.5% of the extract, respectively.

Eunicenone A (**1**) was obtained as a colorless, optically active, oil which analyzed for $C_{29}H_{44}O_4$ by high resolution mass and ^{13}C NMR spectrometric methods. The presence of a linear diterpenoid substituent was readily recognized by familiar ^1H and ^{13}C NMR spectral features, by COSY NMR experiments, and by mass spectral data which showed a typical fragmentation pattern composed of sequential loss of isoprene units. The ^{13}C NMR spectrum of **1** (experimental) showed four vinyl methyl carbons at δ 17.7, 16.2, 16.1, and 16.1 which allowed the trisubstituted double bonds of the terpene unit to be assigned *E* configurations. The mass spectrum of **1** showed a significant fragment at m/z = 183 which analyzed for $C_9H_{11}O_4$ by high resolution mass analysis. This fragment was interpreted as the loss of a $C_{20}H_{33}$ diterpene side chain. By difference, eunicenone A was concluded to possess a C_9 component with 4 degrees of unsaturation. Infrared and ^{13}C NMR analysis showed that three of the four unsaturations in eunicenone A were due to the presence of an α, β-unsaturated ketone (δ 197.4 (C); $\nu_{C=O}$ 1680 cm^{-1}), and a methyl ester (δ 171.9 (C) and 51.7 (CH$_3$); $\nu_{C=O}$ 1740 cm^{-1}). In addition, a

Table. ^{1}H and ^{13}C NMR Assignments for the C-1 to C-8 Portions of Eunicenones A and B (**1**, **2**) and Compounds **4** and **6**[a,b]

	1		**2**		**4**		**6**	
C#	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1		197.4		196.5		197.4		154.9
2		133.9		137.8		138.2		120.2
3	6.82 (1H, dd, 4.6, 0.6)	147.0	6.87 (1H, brd, 4.7, 0.9)	142.5	6.84 (1H, dd, 4.8, 0.9)	142.5	7.16 (1H, brd, 7.6)	124.2
4	4.45 (1H, dd, 4.6, 3.4)	66.3	5.43 (1 H, dd, 4.7, 3.4)	68.5	5.43 (1H, dd, 4.8, 3.5)	68.4	6.95 (1H, brd, 7.6)	123.9
5	2.22 (1H, m)	40.8	2.34 (IH, m)	38.6	2.35 (1H, m)	38.6		143.4
6	2.56 (1H, dd, 16.7, 10.0)	39.0	2.58 (1H, dd, 16.8, 10.1)	39.3	2.58 (1H, dd, 16.8, 10.2)	39.2	6.93 (1H, brs)	110.7
	2.40 (1H, dd, 16.7, 3.9)		2.49 (1H, dd, 16.8, 4.4)		2.48 (1H, dd, 16.8, 4.3)			
7	3.22 (2H, AB)	35.0	3.24 (2H, AB)	35.1	3.22 (2H, AB)	34.8	3.69 (2H, s)	34.2
8		171.9		176.4		171.0		174.5
OAc			2.10 (3H, s)	169.7	2.10 (3H, s)	170.4		
				20.2		20.9		
OMe	3.68 (3H, s)	51.7			3.68 (3H, s)	52.1		

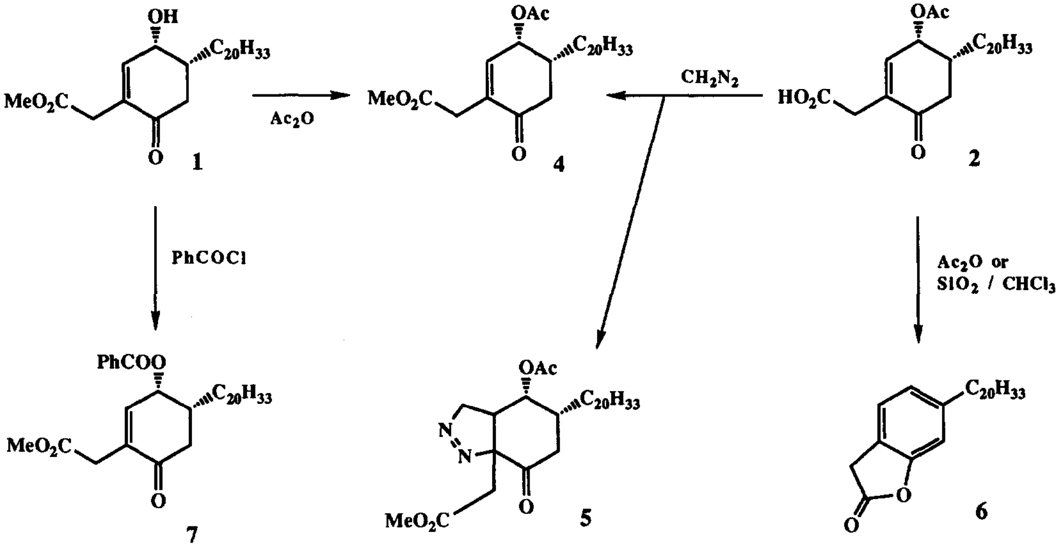
[a] ^{1}H NMR spectra were recorded in $CDCl_3$ solution at 360 MHz. Chemical shifts are reported in δ values (ppm downfield from Me_4Si). *J* values are reported in Hz. Assignments are by decoupling and COSY experiments. [b] ^{13}C NMR spectra for **1** and **2** were obtained in C_6D_6 solution at 50 MHz. Spectra for **4** and **6** were obtained in $CDCl_3$ solution. Carbon multiplicities were determined by DEPT experiments. Assignments for **1** are based upon XHCORR and COLOC (6 Hz) experiments. Assignments for **2**, **4** and **6** are by comparison with eunicenone A (**1**).

secondary alcohol functionality was also observed (δ 66.3 (CH); $\nu_{O\text{-}H}$ 3420 cm^{-1}). Thus, all of the four oxygens in the molecular formula of **1** were confidently assigned.

Comprehensive NMR analysis (Table) allowed the formulation of the C_9 component of eunicenone A as a cyclohexenone ring with substituents at C-2, C-4 and C-5. The C-3 olefinic proton (δ 6.82) was coupled to the C-4 α-hydroxyl proton at δ 4.45, which was in turn coupled to the C-5 proton at δ 2.22. The C-5 position was confirmed as the location of the linear diterpene substituent since this proton was coupled to two mutually coupled allylic protons (δ 2.29 and 2.15) assigned to the C-1' position of the diterpene chain. The proton at C-5 was also coupled to both C-6 protons (δ 2.56 and 2.40). The C-3 olefinic proton was found to be allylically coupled (J = 0.6 Hz) to a two-proton AB signal at δ 3.22 assigned to the C-7 methylene. XHCORR data allowed all protons to be precisely matched to their corresponding carbons. COLOC data, which illustrated coupling between the ester carbonyl at δ 171.9 and the protons at δ 3.68 and 3.22, fixed the position of the methyl ester at C-8. Also, the C-2 olefinic carbon (δ 133.9) was coupled to the C-7 protons at δ 3.22. Using these data, eunicenone A (**1**) was confidently assigned to a unique C_{28} carbon skeleton.

Eunicenone B (**2**) was isolated as an optically active oil which analyzed for $C_{30}H_{44}O_5$ by high resolution mass and ^{13}C NMR spectrometric methods. The overall spectral data of **2** were very similar to those derived from **1**. However, there were several significant differences which allowed **2** to be assigned as the free carboxylic acid and C-4 acetate derivative of **1**. The IR spectrum of **2** showed broad absorption bands between 3500 and 2500 cm^{-1}, as well as an intense carbonyl absorption at 1715 cm^{-1}. Another carbonyl band at 1740 cm^{-1} suggested the presence of an ester. These data, taken in conjunction with the corresponding NMR bands (Table) supported the proposed relationship of **2** with eunicenone A. The structure of eunicenone B was subsequently confirmed by simple chemical conversions (Figure 1). Treatment of eunicenone A (**1**) with acetic anhydride in pyridine

Figure 1. Chemical Transformations of Eunicenones A and B.

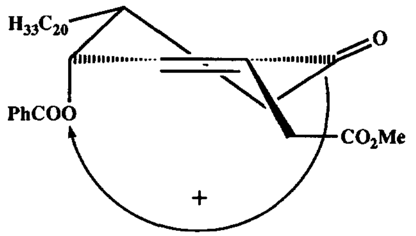


provided the acetate **4** as the sole product in high yield. The acetate **4** was fully characterized by NMR methods (Table). Treatment of eunicenone B (**2**) with diazomethane in ether gave the acetate **4** and compound **5** as the major products. The spectral data of acetate **4**, derived from two different precursors (**1** and **2**), were identical. Also, the structure of **5** was assigned by spectral analysis as the diazomethane 2 + 3 cycloaddition product of the conjugated enone of **4** (experimental section). Thus, eunicenones A and B were confirmed as esterification isomers through mutual conversion to derivative **4**.

The relative and absolute stereochemistry of eunicenones A and B was assigned by a combination of NMR methods and by a CD measurement. Analysis of the vicinal coupling constants between the C-5 proton and the C-6 methylene protons in eunicenone A ($J_{5ax\text{-}6ax}$ =10.0 Hz; $J_{5ax\text{-}6eq}$ = 3.9 Hz) revealed that the C-5 proton is pseudo-axial on the cyclohexenone ring. The small coupling observed (J = 3.4 Hz) between the C-4 and C-5 protons allowed the C-4 proton to be assigned in a pseudo-equatorial position. This configuration was further indicated by its reactivity toward elimination. Eunicenone B was very unstable in both basic and acidic media. Treatment of **2** with acetic anhydride in pyridine gave lactone **6** as the major product (Figure 1). Compound **6** was also produced when **2** was stirred with silica gel in chloroform. Compound **6**, an oil, analyzed for $C_{28}H_{38}O_2$ by high resolution mass and ^{13}C NMR spectrometry, and was defined by comprehensive spectral analyses (Table). It is apparent that the formation of **6** proceeds via elimination of the C-4 acetate and lactone cyclization through the C-1 enol. It is well known that allylic cyclohexenone acetates readily eliminate when the orientation of the acetoxyl group is pseudo-axial. Therefore, the relative configurations are 4-α-hydroxy-5-α-geranylgeranyl.

The absolute stereochemistry of the asymmetric centers in **1** and **2** were determined by a circular dichroism (CD) measurement of the benzoate derivative **7** of eunicenone A. The 4-hydroxyl cyclohexenone moiety of **1** is analogous with that in (+)-dehydrovomifoliol, and its derivative 4-hydroxy-2,6,6-trimethylcyclohexenone-4-benzoate, the absolute stereochemistries of which have been confidently determined by CD measurements.[13, 14] Treatment of **1** with benzoyl chloride in pyridine / DMAP gave benzoate **7** in only modest yield. The UV spectrum (MeOH) of **7** showed an absorption maximum at 231 nm (ε 15500). The CD spectrum (MeOH) showed a maximum at 234 nm (+ 29.1) corresponding to the first Cotton effect (Figure 2). However, the second Cotton effect which was the weaker, was buried in a strong positive background ellipticity. It is not unusual for CD spectra to show very disproportionate maxima or only one maximum.[14] Since the position (234 nm) of the

Figure 2. Absolute Stereochemistry of Eunicenone A Benzoate (7) by CD Methods.



UV (MeOH): 231 nm (ε 15,500)

CD (MeOH): 217 nm (+1.56)
234 nm (+29.1)
324 nm (-0.41)

first Cotton effect was very near to that expected (235 nm), the CD of **7** was assigned as a positive split Cotton effect. On the basis of these observations, the absolute stereochemistry of the asymmetric centers at C-4 and 5 are proposed as 4**R** and 5**R** for both compounds **1** and **2**.

Terpenoid quinones and hydroquinones of mixed biosynthesis are generally assumed to be derived by the combination of a terpenoid and a phenylalanine precursor. By far, the vast majority of these compounds contain either C_6 or C_7 quinoid phenylalanine-derived residues. The structures of the eunicenones support this proposed biosynthesis in that 8 of the 9 original phenylalanine carbons remain.

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EXPERIMENTAL

General. Infrared spectra were recorded on a Perkin-Elmer model 783 spectrophotometer. Ultraviolet spectra were obtained in methanol using a Beckman Acta XIV spectrophotometer. ^1H NMR and COSY spectra were recorded in $CDCl_3$ solutions on a 360-MHz ^1H NMR spectrometer constructed from an Oxford narrow-bore magnet and a Nicolet Fourier transform data system. All chemical shifts are reported with respect to internal Me_4Si. ^{13}C NMR spectra, direct (XHCORR), and long-range (COLOC) carbon-proton correlation spectra were recorded in $CDCl_3$ and C_6D_6 solutions on an IBM WP-200 SY (50 MHz) spectrometer. All chemical shifts are reported with respect to Me_4Si. Mass measurements were supplied by the Mass Spectrometry Center, University of California, Riverside. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter with a 10-cm microcell. CD measurements were performed on a Cary 61 spectropolarimeter with a 0.02 cm cell by signal-averaging 20 scans. All solvents used were spectral grade or were distilled from glass prior to use.

Collection, Extraction and Isolation. *Eunicea* sp.(specimen number CI86-193) was collected by hand using SCUBA at 20 to 25 m depth in July, 1986, in the Tobago Cays, eastern Caribbean Sea. The collection was surface air-dried in the shade and immediately frozen. The gorgonian was defrosted and repeatedly extracted with CH_2Cl_2 and the combined extracts were evaporated to yield 25 g of crude organic materials (from 1.5 kg, dry weight of the gorgonian). Compounds **1** and **2** were purified by silica flash column chromatography eluting with 60-100% EtOAc in isooctane. Further purification by reversed-phase HPLC with 95% MeOH in water (Dynamax C-18 column) yielded **1** and **2** as viscous oils.

Eunicenone A (1). Eunicenone A (**1**, 240 mg) was isolated as a viscous oil by reversed-phase HPLC (95% MeOH in water) as 1% of the crude extract. Eunicenone A (**1**) showed $[\alpha]_D$ +39.8° (c 1.3, $CHCl_3$) and displayed the following spectral features; HRMS: M+, m/z obsd 456.3227, $C_{29}H_{44}O_4$ required 456.3239 $[M-C_{20}H_{33}]^+$, m/z obsd 183.0662, $C_9H_{11}O_4$ required 183.0657; low-resolution MS: m/z (relative intensity) 456 (35), 319 (8), 205 (11), 204 (17), 183 (6), 179 (14), 167 (27), 149 (24), 137 (31), 136 (49), 95 (21), 93 (25), 81 (57), 69 (100); IR (film) 3420, 2920, 1740, 1680, 1440, 1380, 1170, 1110 cm^{-1}; UV (MeOH) 225 nm (sh, ε 10900); ^1H NMR ($CDCl_3$) δ 6.82(1 H, dd, 4.6, 0.6), 5.18-5.05 (4H, m), 4.45 (1 H, dd, 4.6, 3.4), 3.68 (3 H, s), 3.22 (2 H, AB), 2.56 (1 H, dd, 16.7, 10.0), 2.40 (1 H, dd, 16.7, 3.9), 2.29 (1 H, m), 2.22 (1 H, m), 2.15-1.90 (13 H, m), 1.68 (3 H, brs), 1.63 (3 H, brs), 1.60 (9 H, brs); ^{13}C NMR (C_6D_6) δ 197.4 (C), 171.9 (C), 147.0 (CH), 137.4 (C), 135.2 (C), 135.0 (C), 133.9 (C), 131.1(C), 124.9 (CH), 124.8 (CH), 124.7 (CH), 122.1 (CH), 66.3 (CH), 51.7 (CH3), 40.8 (CH), 40.3 (CH2), 40.2 (CH2) x 2, 39.0 (CH2), 35.0 (CH2), 28.7 (CH2), 27.2 (CH2), 27.1(CH2), 27.0 (CH2), 25.8 (CH3), 17.7 (CH3), 16.2 (CH3), 16.1 (CH3) x 2.

Eunicenone B (2). Eunicenine B (**2**, 350 mg) was isolated as a viscous oil by reversed-phase HPLC (95% MeOH in water) as 1.5% of the crude extract. Eunicenone B showed $[\alpha]_D$ +101° (c 0.8, $CHCl_3$) and displayed the following spectral features; HRMS: M+, m/z obsd 484.3177, $C_{30}H_{44}O_5$ required 484.3189; low-resolution MS: m/z (relative intensity) 484 (21), 204 (13), 137 (22), 136 (47), 135 (28), 123 (23), 93 (23), 81 (49), 69 (100), 49 (21); IR (film) 3400-2500 (broad), 2920, 1740, 1715, 1685, 1440, 1370, 1230, 1030 cm^{-1}; UV (MeOH) 225 nm (sh, ε 9900); ^{1}H NMR ($CDCl_3$) δ 6.87 (1 H, dd, 4.7, 0.9), 5.43 (1 H, dd, 4.7, 3.4), 5.15-5.00 (4 H, m), 3.24 (2 H, AB), 2.58 (1 H, dd, 16.8, 10.1), 2.49 (1 H, dd, 16.8, 4.4), 2.34 (1 H, m), 2.22 (1 H, m), 2.10 (3 H, s), 2.05-1.90 (13 H, m), 1.68 (3 H, brs), 1.60 (9 H, brs), 1.57 (3 H, brs); ^{13}C NMR (C_6D_6) δ 196.5 (C), 176.4 (C), 169.7 (C), 142.5 (CH), 137.8 (C), 135.7 (C), 135.3 (C), 135.0 (C), 131.1 (C), 124.9 (CH), 124.8 (CH), 124.5 (CH), 121.2 (CH), 68.5 (CH), 40.2 (CH2) x 3, 39.3 (CH2), 38.6 (CH), 35.1 (CH2), 28.5 (CH2), 27.2 (CH2), 27.1 (CH2), 27.0 (CH2), 25.8 (CH3), 20.2 (CH3), 17.7 (CH3), 16.1 (CH3) x 3.

Eunicenone A Acetate (4). Acetic anhydride (0.5 ml) in 1 ml of dry pyridine was added to a stirred solution of 14 mg (0.03 mmol) of **1** at RT. After stirring for 2 hrs, pyridine and excess anhydride were removed under vacuum. The acetate **4** was obtained (>95% yield) as a viscous oil which showed the following spectral data; HRMS: M^+ m/z obsd 498.3351, $C_{31}H_{46}O_5$ required 498.3345; low-resolution MS: m/z (relative intensity) 498 (32), 204 (14), 167 (47), 137 (22), 136 (39), 107 (26), 93 (26), 81 (50), 69 (100), 43 (25); IR (film) 2920, 1740, 1730, 1685, 1440, 1375, 1240, 1170, 1020 cm^{-1}; UV (MeOH) 224 nm (sh, ε 12500); ^{1}H NMR ($CDCl_3$) δ 6.84 (1H, dd, 4.8, 0.9), 5.43 (1 H, dd, 4.8, 3.5), 5.13-5.05 (4 H, m), 3.68 (3 H, s), 3.22 (2 H, AB), 2.58 (1 H, dd, 16.8, 10.2), 2.48 (1 H, dd, 16.8, 4.3), 2.35 (1 H, m), 2.21 (1 H, m), 2.10 (3 H, s), 2.10-1.95 (13 H, m), 1.68 (3 H, brs), 1.60 (9 H, brs), 1.58 (3 H, brs); ^{13}C NMR ($CDCl_3$) δ 197.4 (C), 171.0 (C), 170.4 (C), 142.5 (CH), 138.2 (C), 135.8 (C), 135.3 (C), 134.9 (C), 131.2 (C), 124.4 (CH), 124.2 (CH), 123.9 (CH), 120.3 (CH), 68.4 (CH), 52.1(CH3), 39.7 (CH2) x 3, 39.2 (CH2), 38.6 (CH), 34.8 (CH2), 28.4 (CH2), 26.8 (CH2), 26.6 (CH2) x 2, 25.7 (CH3), 20.9 (CH3), 17.7 (CH3), 16.1 (CH3), 16.0 (CH3) x 2.

Treatment of Eunicenone B (2) with Diazomethane. A solution of 26 mg (0.05 mmol) of **2** in 2 ml of THF and 12.4 mg (0.08 mmol) of 1-methyl-3-nitronitrosoguanidine (MNNG) were combined in a diazomethane generator. To prevent vigorous reaction, the bottom half of the apparatus was cooled with ice. Dropwise addition of 1 ml of 5 N NaOH initiated diazomethane production. After 20 min, the solvent was removed under vacuum and the products were separated by silica HPLC (30% EtOAc in isooctane). The reaction yielded 11.2 mg (0.02 mmol, 45% yield) of **4** and 10.6 mg (0.02 mmol, 39%) of **5**. The proton and carbon NMR spectra of **4** were identical to those from the compound obtained from the acetylation of **1**. Compound **5** was obtained as an oil which exhibited the following spectral features; low resolution MS : m/z (relative intensity) 540 ($C_{32}H_{48}N_2O_5$, 9), 217 (14), 193 (14), 181 (100), 155 (12), 154 (42), 149 (51), 147 (12); IR ($CHCl_3$) 2970, 2920, 2400, 1730, 1520, 1435, 1040, 845 cm^{-1}; UV (MeOH) no λmax; ^{1}H NMR ($CDCl_3$) δ 5.15-5.05 (3 H, m), 4.97 (1 H, brt, 6.9), 4.87 (1 H, dd, 19.1, 9.0), 4.75 (1 H, dd, 19.2, 2.8), 4.60 (1 H, brs), 3.65 (3 H, s), 3.30 (1 H, d, 16.8), 2.97 (1 H, brd, 9.0), 2.45 (1 H dd, 17.4, 7.9), 2.33 (1 H, dd, 17.5, 10.8), 2.09 (3 H, s), 2.10-1.94 (16 H, m), 1.68 (3 H, s), 1.60 (9 H, s), 1.53 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 201.6 (C), 170.2 (C), 170.1 (C), 138.2 (C), 135.4 (C), 135.1 (C), 131.1 (C), 124.9 (CH), 124.7 (CH), 124.4 (CH), 121.0 (CH), 99.1 (C), 83.0 (CH2), 71.9 (CH), 51.2 (CH3), 40.8 (CH), 40.2 (CH2) x 2, 40.0 (CH2), 39.6 (CH2), 35.7 (CH2), 33.3 (CH), 30.6 (CH2), 27.2 (CH2), 27.1 (CH2), 26.9 (CH2), 25.8 (CH3), 20.7 (CH3), 17.7 (CH3), 16.1 (CH3) x 2, 15.9 (CH3).

Conversion of Eunicenone B (2) to 6. Eunicenone B (**2**) was unstable in both acidic and basic media. Standard work-up of an attempted acetylation reaction (acetic anhydride in pyridine) resulted in extensive decomposition and the formation (in ca. 40% yield) of **6** as the major product. Also, **2** was observed to convert to **6** when a chloroform solution was stirred overnight at room temperature with TLC grade silica gel. Compound **6** was optically inactive $[a]_D$ 0^o (c 0.5, $CHCl_3$)], and exhibited the following spectral features; HRMS: M+ m/z obsd 406.2861, $C_{28}H_{38}O_2$ required 406.2872; low-resolution MS: m/z (relative intensity) 406 (31), 337 (6), 173 (24), 147 (22), 136 (58), 123 (28), 81 (50), 69 (100), 41 (24); IR (film) 2920, 1810, 1630, 1595, 1500, 1435, 1385, 1060, 960 cm^{-1}; UV (MeOH) 280 (ε 6000), 274 (ε 5900), 217 nm (ε 34000); ^{1}H NMR ($CDCl_3$) δ 7.16 (1 H, brd, 7.6), 6.95 (1 H, brd, 7.6), 6.93 (1 H, brs), 5.30 (1 H, brt, 7.9), 5.15-5.08 (3 H, m), 3.69 (2 H, s), 3.36 (2 H, d, 7.2), 2.15-1.95 (12 H, m), 1.71 (3 H, brs), 1.68 (3 H, brs), 1.60 (6 H, brs), 1.56 (3 H, brs); ^{13}C NMR ($CDCl_3$) δ 174.5 (C), 154.9 (C), 143.4 (C), 137.1 (C), 135.2 (C), 134.9 (C), 131.2 (C), 124.4 (CH), 124.2 (CH) x 2, 123.9 (CH) x 2, 122.2 (CH), 120.2 (C), 110.7 (CH), 39.7 (CH2) x 3, 34.2 (CH2), 32.9 (CH2), 26.8 (CH2), 26.6 (CH2), 26.5 (CH2), 25.7 (CH3), 17.7 (CH3), 16.2 (CH3), 16.0 (CH3) x 2.

Formation of Benzoate 7. A molar excess of benzoyl chloride was added to a solution of 32 mg (0.07 mmol) of eunicenone A (**1**) in 1 ml of pyridine containing a catalytic quantity of 4-dimethylaminopyridine. The solution was stirred at 40° overnight. Two ml of THF and few drops of water were then added and the mixture was stirred for 12 hr. After removing excess solvents under vacuum, 20 ml of CH_2Cl_2 and 20 ml of water were added. The CH_2Cl_2 layer was washed with saturated $NaHCO_3$ (15 ml x 2), water (15 ml x 2) and dried under vacuum. Purification by silica HPLC (30% EtOAc in isooctane) gave 12.9 mg (0.02 mmol, 33% yield) of **7**. The benzoate **7** showed the following spectral features; ^{1}H NMR (C_6D_6): δ 8.10 (2 H, d, 7.3), 7.11 (1 H, m), 7.05 (2 H, m), 6.56 (1 H, d, 4.3), 5.59 (1 H, t, 3.5), 5.35-5.20 (3 H, m), 4.98 (1 H, m), 3.30 (3 H, s), 3.06 (2 H, AB), 2.58 (1 H, dd, 16.6, 9.2), 2.28 (1 H, dd, 16.5, 3.3), 2.25-1.99 (15 H, m), 1.68 (3 H, s), 1.62 (6 H, s), 1.57 (3 H, s), 1.44 (3 H, s); UV (MeOH): 231 nm (ε 15,500); CD (MeOH): 217 (+1.56 MD), 234 (+29.1 MD), 324 nm (-0.41 MD).

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