A solution of **43a** and **43b** (63 mg, 0.214 mmol) in a mixture of acetone (4.4 mL), water (14 μL), and concentrated H_2SO_4 (21 μL) was stirred at room temperature for 30 min. Solid $NaHCO_3$ was added, the solvent was removed, and the residue was extracted with ether (5 × 15 mL), washed with brine, and dried. Removal of the solvent yielded a crude (51 mg), which was purified by medium-pressure column chromatography on silica H to afford pure (±)-muzigadial **1a** (40 mg, 76%) and (±)-*epi*-muzigadial **1b** (4 mg, 7%).

1a: mp 115–118 °C (lit.[7a] mp 122–124 °C); IR (CCl_4) 3480, 3095, 1725, 1690, 1638, 1260, 905, 892 cm^{-1}; UV (MeOH) λ_{max} 223.4 nm (ε 5340) [lit.[7a] λ_{max} 223 nm (ε 5300)]; ^1H NMR (80 MHz, $CDCl_3$) δ 0.88 (s, 3 H), 1.09 (d, J = 6.4 Hz, 3 H), 1.3–2.3 (6 H), 2.55 (d, J = 3.0 Hz, 2 H), 4.06 (s, 1 H), 4.77 (s, 1 H), 4.95 (s, 1 H), 7.34 (dd, J = 3.2, 2.4 Hz, 1 H), [in $(CD_3)_2CO$] 9.46 (s, 1 H), 9.66 (s, 1 H); MS, m/z (relative intensity) 230 (3), 219 (100), 177 (12), 159 (13), 145 (10), 135 (26), 131 (12), 117 (12), 107 (23), 105 (17), 93 (14), 91 (29), 77 (15), 43 (11); MS CI (isobutane), m/z (relative intensity) 249 (M^+· + 1, 100), 231 (20), 219 (5); exact mass calcd for $C_{15}H_{20}O_3$ 248.141235, found 248.141235.

1b: mp 104–105 °C; IR (CCl_4) 3440, 1710, 1680, 1635, 1260, 895 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 (s, 3 H), 1.08 (d, J = 6.4 Hz, 3 H), 1.4–2.4 (6 H), 2.52 (d, J = 2.4 Hz, 2 H), 3.54 (s, 1 H), 4.75 (s, 1 H), 4.93 (s, 1 H), 7.16 (dd, J = 4.8, 2.8 Hz, 1 H), 9.35 (s, 1 H), 9.92 (s, 1 H); MS, m/z (relative intensity) 219 (100), 177 (11), 135 (22), 107 (13), 91 (17), 77 (13), 55 (11), 43 (15); MS CI (isobutane), m/z (relative intensity) 249 (M^+· + 1, 100), 231 (20), 219 (8), 203 (8).

As expected, the NOE between the angular methyl and the nonconjugated aldehyde group was 14% for (±)-muzigadial (**1a**) and null for its epimer **1b**.

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Neviotine-A, a New Triterpene from the Red Sea Sponge *Siphonochalina siphonella*

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The structure of a new triterpene neviotine-A (**3**) from the Red Sea sponge *Siphonochalina siphonella* was elucidated by chemical transformations and mainly on the basis of an INADEQUATE 2D NMR experiment. Neviotine-A possesses a new pentacyclic skeleton related to the sipholanes and siphonellanes previously isolated from the same sponge.

The Red Sea sponge *Siphonochalina siphonella* contains an unusually large amount of secondary metabolites,[1-3] the majority of which are triterpenoids of four new types. Structures of two of these, the sipholanes (e.g., **1**)[1,2] and siphonellanes (e.g., **2**),[3] have already been described by us (Figure 1). The structure of a compound belonging to the third type, and designated neviotine-A after the place of collection (Nevi'ot), is the subject of this report. All four new groups have in common the perhydrobenzoxepine moiety.

Neviotine-A (**3**) was purified by repeated chromatography on silica gel and Sephadex LH-20 columns (0.27%, dry weight) and finally by crystallization from acetone–benzene. Neviotine-A revealed the following physicochemical properties: mp 231–233 °C; α_D −50° (c 4.0, $CHCl_3$); MS, (CI) m/e (relative intensity) 507 (M^+) + 1, $C_{30}H_{50}O_6$, 2), (HREI) 488.3513 ($M^+ - H_2O$, $C_{30}H_{48}O_5$, 6.8); IR ν_{max} 3370 (OH), 1705 (CO) cm^{-1}. The ^1H NMR spectrum of **3** disclosed the presence of seven methyl groups (five singlets and two doublets) and five downfield protons, two of which were exchangeable (two additional OH protons are out of sight), while the ^{13}C NMR spectrum revealed seven CH_3's, nine CH_2's, seven CH's, and seven C atoms, thus accounting altogether for 30 carbons and 46 protons out of 50 (see Table I). Addition of trichloracetyl isocyanate (TAI) to a solution of **3** in $CDCl_3$ caused the appearance of four NH singlets at δ 9.18, 8.79, 8.22, and 8.20,[4] thus proving that the remaining four protons of the empirical formula belonged to OH groups. The downfield shift of two signals at δ 4.19 and 5.05 to 5.17 and 5.71 on addition of TAI and the formation of a diacetate **4** indicated that two of the hydroxyls were secondary. In purified $CDCl_3$, these two signals appeared as doublets coupled to two OH doublets at δ 3.42 (d, J = 8 Hz) and 3.48 (d, J = 4 Hz) and collapsed to singlets on addition of D_2O. The appearance of two NH signals on addition of TAI to a solution of **4** in $CDCl_3$ revealed, as expected, the presence of two tertiary hydroxyls which quite rapidly underwent elimination: the 19-OH in 10 min, to give exclusively the 19(20) double bond (vide infra), and the 15-OH after 3.5 h, to give all three possible isomeric olefins.

The location of the two secondary hydroxyls of **3** in positions α and α′ to a ketone, was suggested by the results of a $NaBH_4$ reduction which resulted in the two epimeric

(1) Shmueli, U.; Carmely, S.; Groweiss, A.; Kashman, Y. *Tetrahedron Lett.* **1981**, *22*, 709.
(2) Carmely, S.; Kashman, Y. *J. Org. Chem.* **1983**, *48*, 3517.
(3) Carmely, S.; Loya, Y.; Kashman, Y. *Tetrahedron Lett.* **1983**, *24*, 3673.
(4) Addition of TAI to a solution of sipholenol-A in $CDCl_3$ has shown NH signals at δ_H 8.18 (s) and 8.25 (s).

0022-3263/86/1951-0784$01.50/0

Table I. ^1H, ^{13}C, and H-C Correlation of Neviotine-A (3) in $CDCl_3$ + CD_3OD

C	δ_C	mult	δ_H	long-range correlation	"relay"[a] correlation
2	75.92	s		H-3, H-7, CH_3-24, CH_3-25	
3	83.17	d	4.10	CH_3-24, CH_3-25	
4	213.01	s		H-3, H-5	
5	74.59	d	5.10	CH_3-26	
6	43.47	s		H-5, CH_3-26	
7	68.36	d	5.02	CH_3-26	
8	25.83	t	1.43 1.84		
9	36.09	t	1.82 1.88	H-8′, CH_3-27	
10	42.50	s		H-9, H-11, H-14, CH_3-27	
11	54.73	d	1.54	H-5, H-7, CH_3-26, CH_3-27	H-12
12	22.55	t	1.68 1.83		H-11
13	21.48	t	1.69 1.76		
14	62.22	d	1.39	H-12′, CH_3-27	
15	73.76	s		H-16′, H-23, H-23′	
16	36.00	t	1.11 1.65	H-23′	
17	20.38	t	1.35 1.45		H-16, H-16′
18	53.86	d	1.41	H-16′, H-23′, CH_3-31	
19	87.53	s		H-18, H-28, CH_3-29, CH_3-30	
20	35.55	t	1.71 1.82	H-21, H21′, H-18, H-28	H-20
21	35.15	t	1.45 2.30	H-23, CH_3-31	H-21
22	41.38	s		H-23, H-23′, CH_3-31	
23	46.49	t	1.46 1.76	H-16′, CH_3-31	
24	21.63	q	1.31	CH_3-25	
25	25.83	q	1.17	H-7, CH_3-24	
26	13.84	q	0.67	H-5, H-11	
27	19.34	q	1.30	H-9, H-9′, H-11, H-14	
28	32.51	d	1.76	CH_3-29, CH_3-30	
29	16.71	q	0.89	H-28, CH_3-30	
30	16.11	q	0.87	H-28, CH_3-29	
31	34.11	q	1.25	H-23	

[a] Relay connectivities between protons and neighbor carbon atoms.[6]

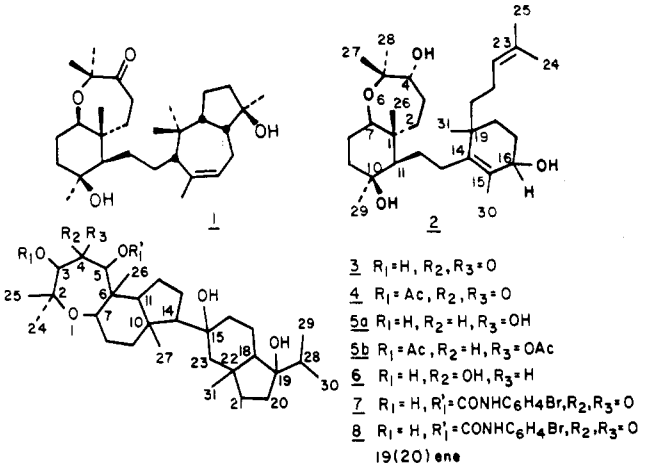


Figure 1.

alcohols **5a** and **6**, both possessing the >CCH(OH)CH(OH)CH(OH)C< functionality as confirmed by double irradiation experiments. Acetylation of the major epimer (**5a**) gave the expected triacetate **5b** (see Experimental Section).

Out of the six unsaturation of **3**, one belongs to the carbonyl group while the rest, in the absence of double bonds, require the presence of five rings. One of the rings has to be a heterocycle formed by an ether bridge linking the remaining two (out of six) sp^3 oxygen-bearing C atoms. Compound **3** contained only seven methyl groups, one less than the eight found in **1** and **2**. Two of the seven are part of an isopropyl radical as shown by irradiation at δ 1.76, which caused collapse of the two methyl doublets at δ 0.87 and 0.89.

The CIMS spectrum shows in addition to the parent peak loss of one to three molecules of water [m/e (relative intensity) 489 ($MH^+ - H_2O$, 23), 471 ($MH^+ - 2H_2O$, 100), 453 ($MH^+ - 3H_2O$, 25)] and also the loss of acetone [449 ($MH^+ - C_3H_6O$, 5)]. Loss of acetone has earlier been found to be characteristic for the perhydrobenzoxepine moiety in the series of **1** and **2**.[2] A similar acetone fragmentation was observed in the HREIMS spectrum in which cleavages of *i*-Pr and Me groups were also seen. This spectrum revealed also cleavages of a $Me_2CCH(OH)CO$ fragment [100 mass units; peaks at m/e (relative intensity) 370.2866 (10.7, $M^+ - 100 - 2H_2O$), 355.2634 (8.2, 370 − Me), and 327.2316 (10.7, 370 − *i*-Pr)] supporting the proposed oxepine moiety. The NMR data (e.g., the signal of H-7) suggest that if the perhydrobenzoxepine moiety is indeed part of **3** it has to possess a conformation different from the one found in **1**.

The most prominent mass spectral fragments were observed at m/e (relative intensity) 293.1744 ($M^+ - C_{13}H_{25}O_4$, 26.7), 211.1678 ($C_{13}H_{23}O_2$, 65), and 193.1581 (211 − H_2O, 51) (see Scheme I). These suggested the presence of a C_{13} moiety that is subject to easy cleavage.

As crystals of **3** itself were found to be unsuitable for X-ray crystallography, we investigated several derivatives for this purpose but to no avail. Inter alia, the very slow reaction of neviotine-A with *p*-bromophenyl isocyanate

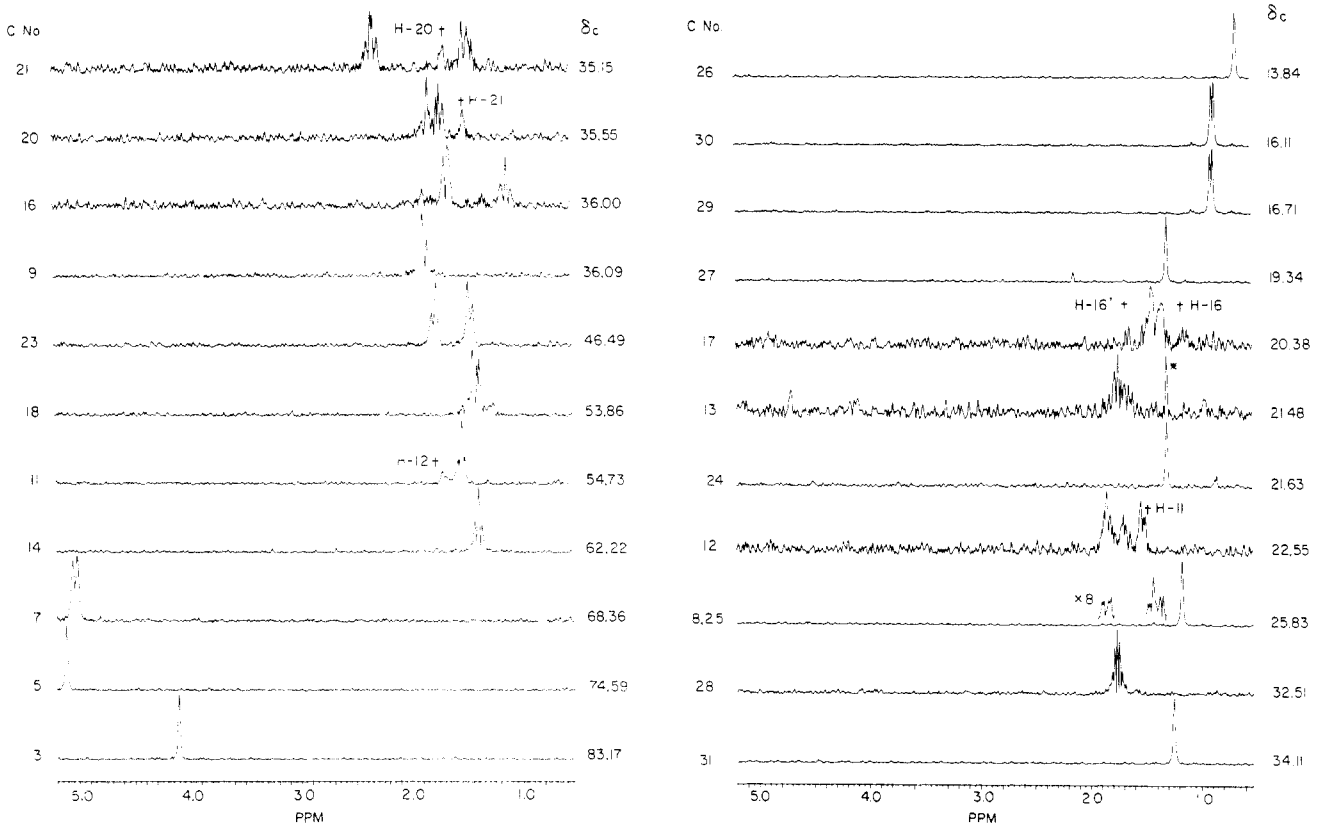
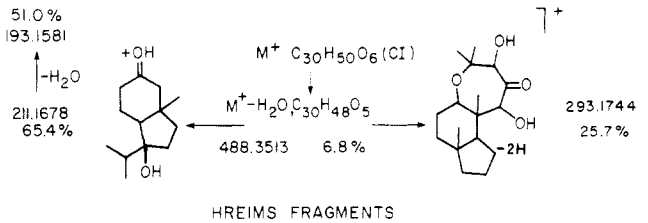


Figure 2. ^{1}H–^{13}C shift correlation spectra (via ^{1}J) of neviotine-A (**3**) presented as a series of cross sections: (†) a "relay" connectivity with the neighbor carbon atom;[6] (*) A residual signal from a vicinal row.

Scheme I. Chemical Ionization and High-Resolution Electron Impact Fragments of Neviotine-A (3)



gave after 7 days at 60 °C two major derivatives: one was the 5-carbamate derivative **7** and the other the 5-carbamate-19(20)-ene **8** (see Experimental Section).

Hence, we turned to 2D NMR techniques for the structure elucidation. Due to considerable overlap in the δ 1.20–1.90 region, the information that could be deduced from a COSY experiment was quite limited. Not much was learned from CH-shift correlations adjusted for ^{1}J (see Figure 2) and also for long-range (^{2}J and ^{3}J) couplings, because of difficulties in distinguishing between ^{2}J and ^{3}J, which precluded determination of the nature of the long-range couplings and, hence, the assignment of the skeleton of **3**. However, collection of the sponge in June 1984 yielded one specimen very rich in **3** which enabled us to purify enough material (ca. 2.5 g) for an INADEQUATE experiment[5] (see Figure 3). Actually two such experiments were performed (each of ca. 72 h), one on a 205 ppm scale and the other, leaving out the carbonyl, in a 77 ppm region. As a result of these measurements all of the C–C bonds except for the C(12)–C(13) and C(20)–C(21) bonds whose shifts are very similar could be established (Table I). The C(12)–C(13) bond was determined from a C–H connectivity between H–12′ and C(14) measured in a long range C–H shift correlation experiment and the C(20)–C(21) band from the observed "relay" (Figure 2).

The latter CH correlation experiment also showed that the ether bridge linked C(2) and C(7) (see Table I for the long-range connectivities), thus confirming the previously suggested oxepine moiety[7] and completing the structure elucidation.

All the other CH correlations (Table I) are in full agreement with the suggested structure and so are the three most priminent peaks in the mass spectrum which result from fragmentations of the C(14)–C(15) bond (Scheme I).

A proposed biogenesis for neviotine-A starting from diepoxy squalene, which is also the suggested precursor of the sipholanes, is shown in Figure 4.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 177 spectrophotometer. Optical rotation was measured on a Perkin-Elmer Model 141 polarimeter using a 10-cm microcell. Low-resolution mass spectra were recorded on a Finnigan-4021 mass spectrometer. High-resolution mass spectra were recorded on a Varian MAT 731 mass spectrometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are reported uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-360 spectrometer, equipped with an Aspect 3000 computer and operating at 360.1 and 90.5 MHz for ^{1}H and ^{13}C, respectively. All chemical shifts are reported with respect to Me_4Si (δ 0).

Isolation of Neviotine-A (3) from *Siphonochalina siphonella*. The sponge *Siphonochalina siphonella* (Levi, 1965) was collected near Nevi'ot in the Gulf of Eilat, in June 1984. The sponge was deep-frozen immediately after collection and then

(5) Bax, A.; Freeman, R.; Kempsell, S. P. *J. Am. Chem. Soc.* **1980**, *102*, 4849.
(6) Bolton, P. H. *J. Magn. Reson.* **1982**, *48*, 336.
(7) A similar CH correlation was also observed in case of sipholenol-A and sipholenone-A: *Magn. Reson. Chem.*, in press.

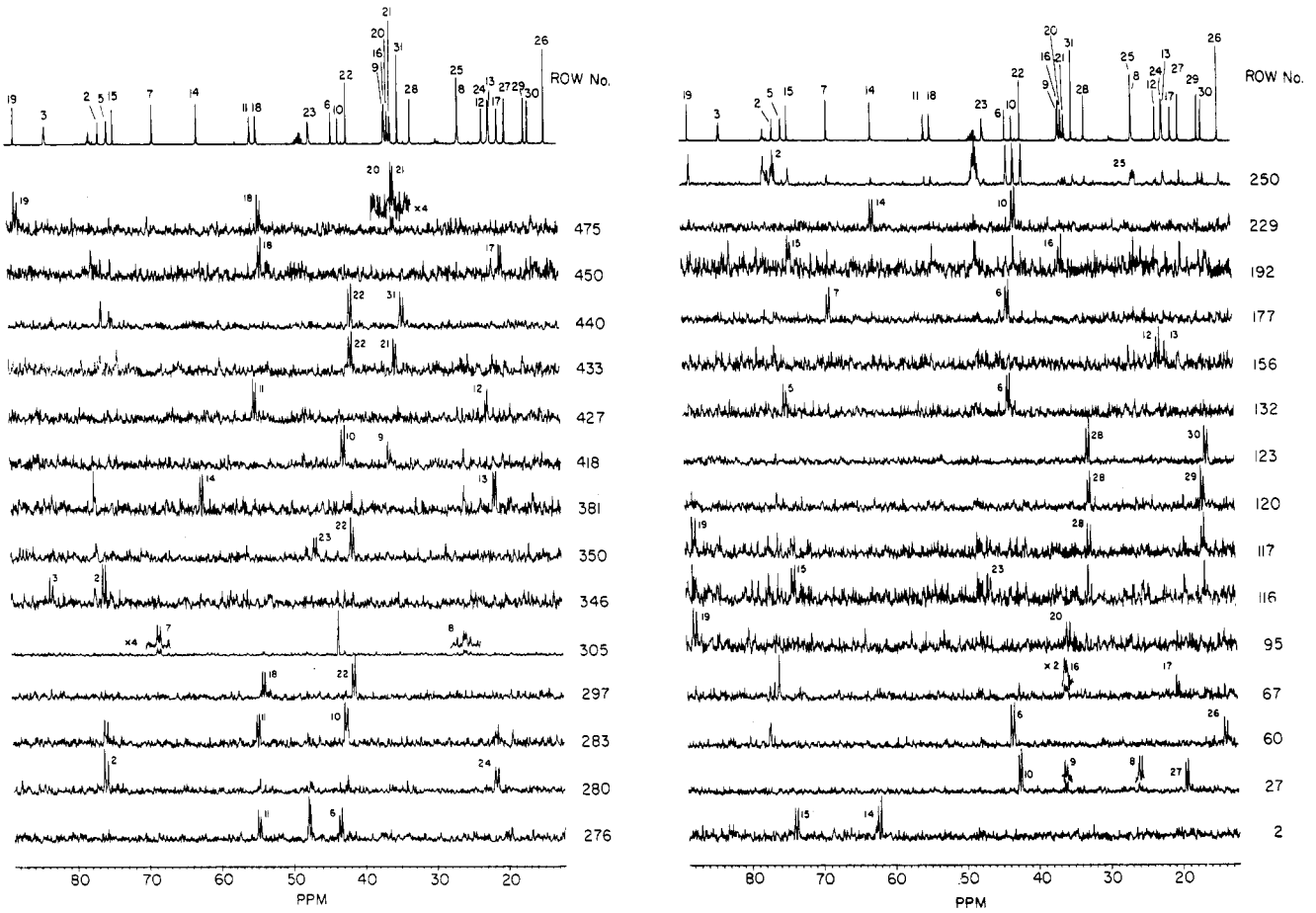


Figure 3. ^{13}C–^{13}C double quantum coherence spectra of neviotine-A (**3**) presented as a series of cross sections. For comparison, the 1D spectrum is presented at the top; residue of this spectrum is seen in row 250. Each matrix row in which the $^{13}C_A$–$^{13}C_B$ pairs of doublets appears was checked to fit the $F_1 = f_A + f_B$ frequency.

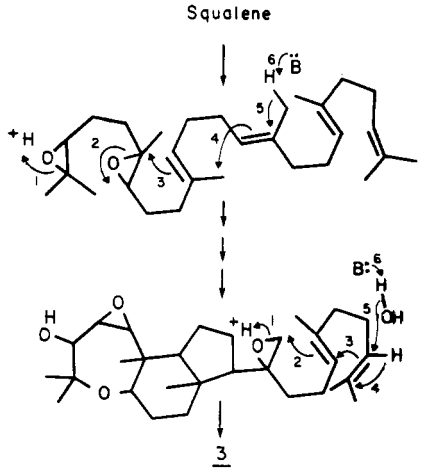


Figure 4. Suggested biogenesis of the neviotanes.

freeze-dried to give the dry material. Dry sponge material (920 g) was extracted with chloroform in a Soxhlet apparatus for 10 h. Evaporation of the solvent gave a brown gum (87 g, 9.45% dry weight).

The crude extract (87 g) was applied in portions of 10 g to a column of Sephadex LH-20, eluted with $CHCl_3$/petroleum ether (65:35). The last fractions from each column were combined and rechromatographed on the same column, and the proper last fractions combined and applied to a column of silica gel H, eluted with solvents of gradually increasing polarity, from $CHCl_3$ through EtOAc.

Neviotine-A (**3**) was eluted from the column with 20% EtOAc in $CHCl_3$ as a colorless foam, which was crystallized from an acetone–benzene mixture to give cubic colorless crystals (2.5 g): mp 231–233 °C; $[\alpha]^{24}_D$ –50° (*c* 4.0, $CHCl_3$); IR ($CHCl_3$) 3380, 2910, 2865, 1705, 1455, 1382, 1255, 1140, 1080, 1040, 960, 910 cm^{-1}; mass spectrum, (CI, isobutane) *m/e* (relative intensity) 507 (MH^+, 2), 489 ($MH^+ - H_2O$, 23), 471 ($MH^+ - 2H_2O$, 100), 453 ($MH^+ - 3H_2O$, 25), 413 (15), 210 (12), 176 (10), (HREI, 70 eV) 489.3539 ($C_{30}H_{49}O_5$, $M^+ - OH$, 2.5), 488.3513 ($C_{30}H_{48}O_5$, $M^+ - H_2O$, 6.8), 470.3373 (20), 455.3190 (16.1), 430.3082 (3.2), 427.2849 (9.3), 370.2866 (10.7), 355.2634 (8.2), 341.2869 (13.6), 327.2316 (10.7), 293.1744 (25.7), 211.1678 (65.4), 193.1581 (51.1), 175.1478 (63.2), 147.1165 (66.8), 135.1174 (100). For ^1H and ^{13}C NMR data, see Table I.

Acetylation of Neviotine-A (3) to Diacetate 4. Treatment of neviotine-A (**3**, 100 mg) with an Ac_2O/pyridine solution (1 mL), at room temperature overnight afforded, after the usual workup, a mixture of products. The residue was flash chromatographed on a short silica gel H column. The main product **4** (65 mg, 56% theoretical) was eluted from the column with 30% EtOAc in petroleum ether: oil; mass spectrum, (CI, isobutane) *m/e* (relative intensity) 591 (MH^+, 25), 573 ($MH^+ - H_2O$, 46), 555 ($MH^+ - 2H_2O$, 100), 533 ($MH^+ - C_3H_6O$, 70), 513 ($MH^+ - H_2O$ – AcOH, 55), 495 ($MH^+ - 2H_2O$ – AcOH, 50); IR ($CHCl_3$) 3470, 2950, 2890, 1755, 1725, 1470, 1380, 1250, 1100, 1045, 975, 920 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.65 (1 H, s), 5.28 (1 H, s), 4.77 (1 H, dd, J = 12.4, 5.4 Hz), 2.31 (1 H, dt, J = 5.5, 12.1 Hz), 2.22 (3 H, s), 2.13 (3 H, s), 1.34 (3 H, s), 1.31 (3 H, s), 1.28 (3 H, s), 1.25 (3 H, s), 0.92 (3 H, s), 0.91 (3 H, d, J = 6.5 Hz), 0.90 (3 H, d, J = 6.7 Hz); ^{13}C NMR (90.5 MHz, $CDCl_3$) δ (mult, C number)[8] 200.54 (s, 4), 170.18 (s, Ac), 168.60 (s, Ac), 88.15 (s, 19), 84.65 (d, 3), 77.70 (d, 5), 76.02 (s, 2), 74.27 (s, 15), 69.34 (d, 7), 62.33 (d, 14), 55.02 (d, 18), 54.80 (d, 11), 47.38 (t, 23), 43.18 (s, 6), 42.04 (s, 10), 41.79 (s, 22), 37.07 (t, 16), 36.73 (t, 20), 36.59 (t, 9), 35.75 (t, 21), 35.03 (q, 31), 32.99 (d, 28), 26.95 (q, 25), 26.70 (t, 8), 22.65 (t, 12), 22.04 (q, 27), 21.93 (t, 13), 20.93 (t, 17), 20.70 (2 x q, Ac), 20.21 (q, 24), 17.43 (q, 30), 16.84 (q, 29), 15.73 (q, 26).

(8) Assignment was obtained from ^1J ^1H–^{13}C shift correlation experiment and comparison with the lines assignment of compound **3**.

Reduction of Compound 3 with Sodium Borohydride To Give Compounds 5a and 6. $NaBH_4$ (100 mg) was added in portions to a solution of **3** (100 mg) in MeOH (10 mL) and the solution stirred at 0 °C for 2 h. The excess of the reagent was destroyed with 10% aqueous AcOH (5 mL). The solvent was then evaporated and the residual water extracted with $CHCl_3$ (3 × 20 mL). The combined $CHCl_3$ phase was dried over anhydrous $MgSO_4$, and the solvent was evaporated. The residue (98 mg) was chromatographed on silica gel H column with increasing percent of EtOAc in $CHCl_3$ as eluant to yield the two isomeric alcohols **5a** and **6**. Compound **5a** the less polar isomer: 75 mg (75%); oil; IR ($CHCl_3$) 3500, 2970, 2890, 1440, 1250, 1192, 1140, 965 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 4.27 (H-5, d, J = 4.7 Hz), 3.96 (H-4, dd, J = 4.7, 10.3 Hz), 3.90 (H-7, dd, J = 3.4, 11.7 Hz), 3.61 (H-3, d, J = 10.3 Hz), 2.29 (H-21$_a$, dt, J = 5.4, 12.1 Hz), 1.33 (CH_3-25, s), 1.25 (CH_3-31, s), 1.18 (CH_3-24, s), 1.05 (CH_3-27, s), 0.96 (CH_3-26, s), 0.90 (CH_3-30, d, J = 6.6 Hz), 0.88 (CH_3-29, d, J = 6.6 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ (mult, C number)[8] 88.22 (s, 19), 76.16 (s, 2), 74.36 (s, 15), 72.82 (d, 3), 71.47 (d, 5), 70.12 (d, 4), 69.42 (d, 7), 62.55 (d, 14), 56.45 (d, 11), 54.95 (d, 18), 47.56 (t, 23), 42.99 (s, 10), 42.85 (s, 6), 42.08 (s, 22), 36.94 (t, 16), 36.79 (t, 20), 36.67 (t, 9), 35.89 (t, 21), 35.06 (q, 31), 33.02 (d, 28), 29.30 (q, 25), 27.01 (t, 8), 22.23 (t, 12), 21.58 (q, 27), 21.47 (t, 13), 21.08 (t, 17), 18.20 (q, 26), 17.46 (q, 30), 17.3 (q, 24), 16.88 (q, 29). Acetylation of compound **5a** (5 mg) gave the triacetyl derivative **5b** (5 mg): oil; IR ($CHCl_3$) 3620, 3480, 2945, 2880, 1745, 1470, 1372, 1260, 1097, 1043, 975, 945, 917, 880 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.51 (1 H, dd, J = 3.6, 7.5 Hz), 5.35 (1 H, d, J = 3.6 Hz), 5.18 (1 H, d, J = 7.5 Hz), 4.25 (1 H, br d, J = 11.0 Hz), 2.31 (1 H, dt, J = 5.3, 12.0 Hz), 2.12 (3 H, s), 2.06 (3 H, s), 2.00 (3 H, s), 1.35 (3 H, s), 1.26 (3 H, s), 1.21 (3 H, s), 1.19 (6 H, s), 0.89 (3 H, d, J = 6.5 Hz), 0.88 (3 H, d, J = 6.5 Hz); mass spectrum, (CI, isobutane) m/e (relative intensity) 617 ($MH^+ - H_2O$, 25), 599 ($MH^+ - 2H_2O$, 57), 557 ($MH^+ - H_2O$ - AcOH, 99), 539 ($MH^+ - 2H_2O$ - AcOH, 100). Compound **6**, the more polar isomer: 17 mg (17%); oil; IR ($CHCl_3$) 3490, 2980, 2890, 1490, 1210, 1100, 1010, 950 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 4.44 (1 H, d, J = 4.8 Hz), 4.21 (1 H, dd, J = 4.7, 9.5 Hz), 3.99 (1 H, dd, J = 3.5, 11.5 Hz), 3.73 (1 H, d, J = 9.5 Hz), 2.29 (1 H, dt, J = 5.4, 12.1 Hz), 1.34 (3 H, s), 1.25 (3 H, s), 1.24 (3 H, s), 1.04 (3 H, s), 0.96 (3 H, s), 0.90 (3 H, d, J = 6.6 Hz), 0.88 (3 H, d, J = 6.6 Hz); mass spectrum, (CI, isobutane) m/e (relative intensity) 491 ($MH^+ - H_2O$, 15), 473 ($MH^+ - 2H_2O$, 100), 455 ($MH^+ - 3H_2O$, 39).

Treatment of Compound 3 with *p*-Bromophenyl Isocyanate To Yield Compounds 7 and 8. A solution of **3** (150 mg) and *p*-bromophenyl isocyanate (100 mg) in dry $CHCl_3$ (25 mL) was kept for 7 days at 60 °C. The $CHCl_3$ was then evaporated and the residue flash chromatographed on a silica gel H column, eluted with $CHCl_3$. Out of eight spots seen on a TLC plate, we purified three: the major and most polar product, **7** (53 mg), the least polar product, **8** (4 mg), and starting material, **3** (56 mg). Compound **7**: amorphous solid; mp 196–199 °C; IR ($CHCl_3$) 3690, 3620, 3540, 3440, 3330, 2940, 2880, 1720, 1710, 1593, 1514, 1400, 1385, 1310, 1240, 1076, 972, 822 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.19 (H-3′ and H-5′, br d, J = 7.8 Hz), 6.96 (H-2′ and H-6′, d, J = 7.8 Hz), 6.95 (NH, br s), 6.06 (H-5, s), 5.95 (HO-3, d, J = 3.7 Hz), 5.15 (H-7, dd, J = 12.3, 3.8 Hz), 3.97 (H-3, d, J = 3.7 Hz), 1.36 (CH_3-27, s), 1.32 (CH_3-24, s), 1.25 (CH_3-31, s), 1.20 (CH_3-25, s), 0.88 (CH_3-29 and CH_3-30, d, J = 6.6 Hz), 0.87 (CH_3-26, s); ^{13}C NMR (90.5 MHz, $CDCl_3$) δ (mult, C number)[8] 210.10 (s, 4) 152.81 (s, $NHCO_2$), 136.53 (s, 4′), 131.52 (d, 3′ and 5′), 120.15 (br d, 2′ and 6′), 116.31 (s, 1′), 88.03 (s, 19), 84.52 (d, 3), 79.16 (d, 5), 76.57 (s, 2), 75.62 (s, 15), 68.81 (d, 7), 62.47 (d, 14), 55.09 (d, 18), 54.95 (d, 11), 46.11 (t, 23), 43.11 (s, 6), 42.03 (s, 10), 41.84 (s, 22), 37.89 (t, 16), 36.99 (t, 20), 36.75 (t, 9), 35.39 (t, 21), 34.64 (q, 31), 32.95 (d, 28), 27.08 (q, 25), 26.31 (t, 8), 23.46 (t, 12), 22.75 (q, 24), 21.84 (t, 13), 21.33 (q, 27), 20.86 (t, 17), 17.45 (q, 29), 16.88 (q, 30), 15.88 (q, 26); mass spectrum, (CI, isobutane) m/e (relative intensity) 707:705 (MH^+, 1:1 5), 689:687 (1:1, 20), 671:669 (1:1, 29), 489 (22), 471 (98), 453 (100). Compound **8**: oil; IR ($CHCl_3$) 3697, 3440, 3300, 2980, 2885, 1720, 1710, 1592, 1515, 1400, 1385, 1310, 1235, 1078, 930, 825 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.24 (2 H, d, J = 8.4 Hz), 7.04 (2 H, d, J = 8.8 Hz), 6.71 (1 H, br s), 6.07 (1 H, s), 5.60 (1 H, br s), 5.15 (1 H, dd, J = 2.7, 12.2 Hz), 5.08 (1 H, br s), 4.03 (1 H, d, J = 3.9 Hz), 2.63 (1 H, br d, J = 12.6 Hz), 2.29 (1 H, br s), 2.23 (1 H, m), 1.38 (3 H, s), 1.34 (3 H, s), 1.19 (3 H, s), 1.05 (3 H, d, J = 6.6 Hz), 0.97 (3 H, d, J = 6.9 Hz), 0.92 (3 H, s), 0.88 (3 H, s); ^{13}C NMR (90.5 MHz, $CDCl_3$) δ 210.05 (s), 152.64 (s), 136.44 (s), 132.01 (s), 131.62 (d × 2), 119.82 (br d × 2), 118.67 (d), 116.31 (s), 84.21 (d), 79.02 (d), 76.67 (s), 75.86 (s), 68.84 (d), 62.34 (d), 54.86 (d), 50.98 (d), 43.66 (s), 43.03 (t), 42.55 (s), 41.84 (s), 40.85 (t), 36.98 (t), 36.96 (t), 32.11 (q), 27.99 (d), 27.02 (q), 26.34 (t), 24.42 (t), 23.50 (t), 22.74 (q), 22.10 (q), 21.81 (t), 21.24 (q), 21.12 (q), 15.80 (q); mass spectrum, (CI, isobutane) m/e (relative intensity) 689:687 (MH^+, 1:1, 29), 671:669 (1:1, 12), 489 (37), 471 (34), 453 (100), 395 (53).

2D NMR experiments have been performed on a Bruker AM-360 spectrometer equipped with an Aspect 3000 computer. The INADEQUATE measurements were carried out by using a 10-mm o.d. sample tube containing 1.8 g of neviotine-A (**3**) in 3 mL of 3:1 $CDCl_3$–CD_3OD solution, and for the ^1H–^{13}C chemical shift correlation measurements, an aliquot of the same solution was placed in a 5-mm o.d. sample tube. 2D ^1H–^{13}C chemical shift correlation experiments have been performed in a 5-mm $^1H/^{13}C$ dual probe, using the regular heteronuclear shift correlation pulse sequence;[9] pulse widths were 6.6 μs for the 90° ^{13}C pulse and 16.2 μs for the decoupler ^1H 90° pulse, and the probe temperature was 300 K.

Three 2D ^1H–^{13}C chemical shift correlation experiments were taken for neviotine-A (**3**), and the first one was set to obtain $^1J_{CH}$ connectivities; a 1-s recycle delay was allowed between each pulse sequence. The time for the development of the polarization transfer $t_1 = 2J^{-1}$ and the refocusing time for antiphase multiplet components $t_2 = 4J^{-1}$ were adjusted to give maximum enhancement for J_{CH} = 135 Hz. Quadrature detection was applied in both directions by using an eight-step phase cycling for N-type peak selection.

The 2D map was obtained with spectral widths of 6849.3 Hz (^{13}C, F_2) and ±862.0 Hz (^1H, F_1) and a data acquisition of 160 scans × 300 increments in t_1. Zero filling in t_1 provided a matrix of 2K × 1K (t_2, t_1) which was transformed into (F_2, t_1) and then (F_2, F_1) using sine bell functions for weighting in both dimensions. The latter processing provided digital resolutions of 6.69 and 1.64 Hz/Pt in F_2 and F_1 domains, respectively.

The two additional ^1H–^{13}C chemical shift correlation experiments were set to give maximum enhancement for J_{HC} = 5 and 10 Hz. The 2D maps were obtained with spectral widths of 18518.5 Hz (^{13}C, F_2) and ±862.1 Hz (^1H, F_1) and data acquisition of 320 scans × 256 increments in t_1. Zero filling in t_1 provided a matrix of 2K × 1K (t_2, t_1) and digital resolution of 18.1 and 1.68 Hz/Pt in F_2 and F_1 domains, respectively. All other acquisition and processing parameters were identical with those described for the other ^1H–^{13}C chemical shift correlation experiment. The INADEQUATE experiments were performed in 10-mm multinuclear probe, using a modified 2D INADEQUATE pulse sequence.[10] The 90° ^{13}C pulse was 14 μs and the probe temperature 300 K.

Two experiments have been taken; in the first one the double quantum coherence data were obtained by using a spectral width of 18518.5 Hz (216.6–12.0 ppm, F_2) and ±8000 Hz (folded, F_1) and in the second 6844.4 Hz (88.7–12.0 ppm, F_2) and ± 3199.0 Hz (folded, F_1). In both experiments a data acquisition of 768 scans × 256 increments in t_1 were used to provide, after zero filling in both dimensions, a matrix of 2K × 512 (t_2, t_1), which were transformed after weighting with sine bell functions in both dimensions. The τ increment was 7.5 ms, corresponding to coupling of 33.3 Hz in both experiments. The t_1 increments were 62.5 and 156.3 μs, respectively, and the pulse repetition times were 2.5 and 1.0 s, respectively.

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