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OXIDATION OF NORDITERPENOID ALKALOIDS WITH OSMIUM TETROXIDE[1]

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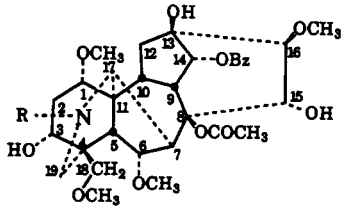
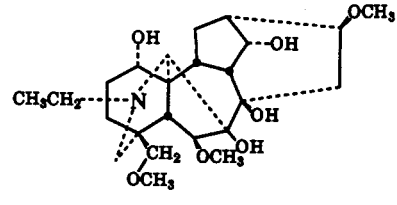
ABSTRACT.—Oxidation of nine norditerpenoid alkaloids possessing two different types of skeletal structures was carried out with osmium tetroxide. This reagent selectively oxidizes oxygenated norditerpenoid alkaloids of the aconitum type [**1**] to an *N*-acyl or *N*-deethyl derivative and of the lycoctonine type [**2**] to a lactam derivative. This oxidation is of diagnostic value in determining the orientation of the C-6 oxygenated functional group.

In a previous communication (1), we reported an unusual room temperature oxidation of pyrodelphinine [**3**] with OsO_4. Besides the expected *cis*-diol **4**, a minor oxidation product **5**, whose structure was confirmed by an X-ray analysis was also isolated. The reaction with OsO_4 was then applied to the alkaloids mesaconitine [**6**] and delphinine [**7**], each containing an *N*-Me group. Mesaconitine afforded oxonitine [**8**] (92%) and delphinine gave α-oxodelphinine [**9**] (75%). Oxidation of the highly oxygenated norditerpenoid alkaloids gives varying results depending on the structure of the alkaloid and the oxidant used (2). Mesaconitine [**6**] is resistant to oxidation with $KMnO_4$ in Me_2CO and HOAc or 5% MeOH in Me_2CO and HOAc at 25° for 5 h. However,



1 R=Et
6 R=Me
8 R=CHO
11 R=H
12 R=Ac



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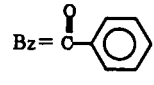

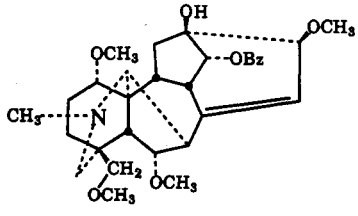

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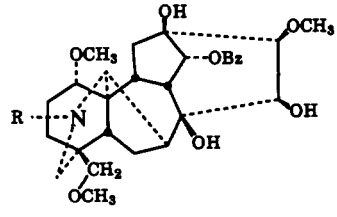


4 R=Me
5 R=CHO

[1]Abstracted in part from the Ph.D. dissertation of H.P. Chokshi, University of Georgia, Athens, Georgia (1985).

when the reaction was carried out at 50° in Me_2CO and HOAc for 48 h, mesaconitine afforded oxonitine [**8**] in 75% yield (3). Similar treatment of delphinine [**7**] with $KMnO_4$ (4) afforded a mixture of α-oxodelphinine [**9**] and β-oxodelphinine [**10**].

With this background information, we were prompted to extend the study of the oxidation with OsO_4 to other tertiary-amine-type norditerpenoid alkaloids.

Reaction of aconitine [**1**] with OsO_4 under the reported conditions (1.3 equivalents of OsO_4, 3.0 h) (1) gave a mixture of products in poor yields. Most of the aconitine was recovered. However, reaction of aconitine with 2.2 equivalents of OsO_4 was complete within 3.0 h, affording *N*-deethylaconitine [**11**] (39%) and *N*-acetyl-*N*-deethylaconitine [**12**] (17.4%). The basic product **11** lacked peaks for the methyl and the methylene groups of *N*-Et at 13.0 and 47.0 ppm, respectively, in the ^{13}C-nmr spectrum (Table 1). The ^1H-nmr spectrum of **11** also supported the structure, as no triplet

TABLE 1. ^{13}C Chemical Shifts[a] and Assignments for Oxonitine [**8**][b], *N*-Deethylaconitine [**11**],[b] *N*-Acetyl-*N*-deethylaconitine [**12**],[b] β-Oxodeltaline [**14**],[c] 14-Acetyl-β-oxodictyocarpine [**17**],[c] *N*-Acetyl-*N*-deethyl-1-dehydrodelphisine [**24**],[c] and *N*-Acetyl-*N*-deethyl-1-*epi*-delphisine [**25**].[c]

Carbon	Compound			Carbon	Compound			
	8	**11**	**12**		**14**	**17**	**24**	**25**
1(d)	83.0	83.2	83.0	1	80.6(d)	80.6(d)	210.3(s)	67.2(d)
2(t)	34.4	34.7	34.7	2	27.0(t)	26.8(t)	39.3(t)	30.7(t)
3(d)	68.7	71.2	69.5	3	39.1(t)	38.1(t)	38.2(t)	29.1(t)
4(s)	43.2	43.3	43.1	4	45.1(s)	45.1(s)	39.1(s)	38.8(s)
5(d)	47.5	47.1	47.1	5	49.7(d)	49.6(d)	53.9(d)	52.8(d)
6(d)	79.5	81.3	80.0	6	75.6(d)	75.4(d)	82.1(d)	82.5(d)
7(d)	42.4	43.7	42.1	7	90.1(s)	90.1(s)	53.7(d)	45.1(d)
8(s)	90.2	91.4	90.7	8	83.4(s)	82.6(s)	85.2(s)	85.4(s)
9(d)	40.5	40.7	40.4	9	49.7(d)	49.2(d)	42.8(d)	42.8(d)
10(d)	38.6	40.7	39.2	10	80.6(s)	80.2(s)	38.5(d)	38.5(d)
11(s)	50.5	50.7	50.3	11	54.0(s)	54.3(s)	60.1(s)	50.0(s)
12(t)	34.9	34.9	33.8	12	34.1(t)	34.1(t)	34.2(t)	28.9(t)
13(s)	74.4	74.1	74.1	13	37.8(d)	36.1(d)	38.8(d)	39.0(d)
14(d)	78.6	78.9	78.8	14	81.3(d)	74.0(d)	75.4(d)	75.3(d)
15(d)	78.9	78.7	78.8	15	34.7(t)	34.6(t)	37.7(t)	37.5(t)
16(d)	90.2	89.7	90.1	16	81.0(d)	80.6(d)	82.6(d)	83.0(d)
17(d)	61.1	61.2	61.2	17	62.5(d)	62.6(d)	56.4(d)	55.7(d)
18(t)	73.3	77.1	74.3	18	22.0(q)	21.8(q)	78.2(t)	79.5(t)
19(t)	49.2	49.2	49.3	19	172.9(s)	172.8(s)	50.3(t)	49.6(t)
1′(q)	57.9	55.7	57.3	N-CH_2(O)	43.0(t)	43.0(t)	169.8(s)	169.9(s)
6′(q)	58.3	57.6	57.7	CH_3	12.4(q)	12.3(q)	22.7(q)	22.7(q)
16′	55.6	55.7	55.5	1′	54.9(q)	54.9(q)	—	—
18′(q)	59.1	59.2	59.1	6′	—	—	58.3(q)	57.9(q)
C=O(8′)(s)	172.2	172.2	172.3	C-7-O				
CH_3(q)	21.3	21.4	21.3	CH_2	94.2(t)	94.1(t)	—	—
N-C=O(s)	163.4	—	170.3	C-8-O				
CH_3(H)(q)	—	—	22.4	14′	57.9(q)	—	—	—
C=O	166.1	166.2	166.0	16′	56.4(q)	56.2(q)	56.7(q)	56.7(q)
1(s)	129.7	129.6	129.9	18′	—	—	59.3(q)	59.2(q)
2(d)	128.6	128.7	128.7	C=O(6′)(14′)	169.5(s)	169.5(s)	169.5(s)	169.5(s)
3(d)	129.4	129.6	129.6	CH_3(q)	21.5(q)	21.3(q)	22.4(q)	22.4(q)
4(d)	133.8	133.4	133.5	C=O(8′)	—	171.7(s)	170.8(s)	170.8(s)
5(d)	129.4	129.6	129.6	CH_3	—	21.5(q)	21.2(q)	21.2(q)
6(d)	128.6	128.6	128.7					

[a]Chemical Shifts are in ppm downfield from TMS. The solvent is $CDCl_3$.
[b]Known compound with chemical shift assignments reported for first time.
[c]New compound.

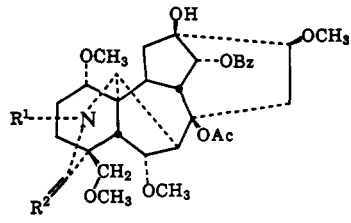
for the methyl of *N*-Et group was observed around 1.00 ppm. The neutral product **12** showed the absence of a triplet at ca. 1.00 ppm for an *N*-Et group, but showed a 3H singlet at 2.35 ppm typical of a methyl of an *N*-acetyl group. In the ^{13}C-nmr spectrum of **12** (Table 1) the appearance of a signal at 170.7 ppm for the *N*-acetyl carbonyl and 22.4 ppm for the corresponding methyl group further supported the structure of the neutral product as *N*-acetyl-*N*-deethylaconitine. In contrast to permanganate, oxidation with OsO_4 did not give any detectable amounts of oxonitine [**8**]. The ^{13}C-nmr spectral chemical shift assignments for *N*-deethylaconitine [**11**], oxonitine [**8**], and *N*-acetyl-*N*-deethylaconitine [**12**] are given in Table 1.

Reaction of deltaline [**13**] with 2.2 equivalents of OsO_4 afforded the crystalline β-oxodeltaline [**14**] (77%). The ^{13}C-nmr spectrum of **14** showed 25 lines for 27 carbon atoms, and off-resonance partial decoupling experiments gave the multiplicity of each signal (Table 1). The signal at 80.6 ppm was attributed to two carbon atoms since in the off-resonance partial decoupling experiments it appeared as one singlet and one doublet. The signal at 172.9 ppm was assigned to the C-19 lactam carbonyl. In the ^{1}H-nmr spectrum of **14**, the typical 3H triplet for the methyl of an *N*-Et group was observed at 1.14 ppm, and no singlet was observed around 2.30 ppm as is expected for the methyl of an *N*-acetyl group. In the ^{13}C-nmr spectrum of **13**, C-4 appears at 33.7 ppm, whereas in that of the product **14** it appears at 45.1 ppm, a result expected due to the β effect of the C-19 carbonyl. The γ effect observed for C-18, C-5, and C-3 also supports this conclusion. These observations eliminate the possibility of an *N*-acetyl group in product **14**. The structure of β-oxodeltaline [**14**] is further supported by its mass spectrum which shows a molecular ion peak at *m/z* 521 $[M]^+$ for the molecular formula $C_{27}H_{39}NO_9$.

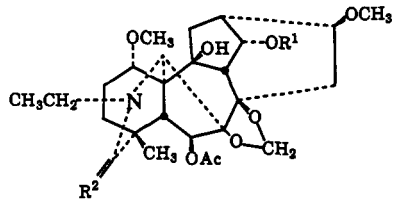
Reaction of 14-acetyldictyocarpine [**16**], prepared by acetylation of dictyocarpine [**15**] (5), with OsO_4 gave a crystalline compound, 14-acetyl-β-oxodictyocarpine [**17**] (60%). Its ^{13}C-nmr spectrum (Table 1) showed a chemical shift of 172.8 ppm for the lactam carbonyl at C-19. A signal at 45.1 ppm for C-4 clearly indicates a C-19 carbonyl due to the β effect on C-4. Furthermore, the ^{1}H-nmr spectrum of **17** clearly eliminates the presence of an *N*-acetyl moiety (δ 1.10, t, 3H, *N*-CH_2CH_3, $J = 7$ Hz). The mass spectrum of the product also supports structure **17** as the molecular ion peak appears at *m/z* 549 $[M]^+$ for $C_{28}H_{39}NO_{10}$.

These experiments clearly demonstrate that lycoctonine-type bases **2**, **13**, and **16**, bearing a β-oxygen substituent at C-6, undergo oxidation at C-19 when treated with OsO_4. The mechanism may involve an initial complexing of OsO_4 with the free pair of electrons on the nitrogen. This intermediate may undergo a trans proton elimination with formation of an iminium ion intermediate, which is rapidly oxidized, most likely via the carbinolamine to the lactam. In fact, treatment of delcosine [**2**], bearing a hydroxyl at C-1 in ring A, with OsO_4 afforded 18-methoxygadesine [**18**] (53.3%), the carbinolamine ether resulting probably by trapping the proposed iminium ion intermediate by the C-1 hydroxyl. The structure of this crystalline carbinolamine ether **18** was assigned on the basis of ^{1}H-nmr, ^{13}C-nmr, and ir spectra. In the ^{13}C-nmr spectrum (Table 1), the new doublet at 68.8 ppm, the singlet at 43.2 ppm, and the γ effect observed on the resonances of C-3, C-5, and C-18 are consistent with a C-1–C-19 inner ether. 18-Methoxygadesine [**18**] is a rare, naturally occurring alkaloid that was isolated by Gonzalez *et al.* (6) from *Consolida orientalis* Gray; its structure was established by X-ray analysis.

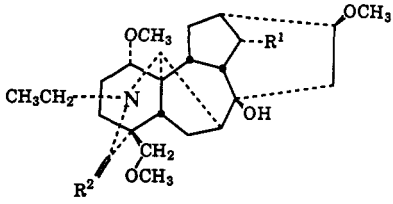
Reaction of talatizamine [**19**], a compound that has no C-6 substituent, with OsO_4 afforded the known (8) β-oxotalatizamine [**20**] (74%), mp 199–200°. Because talatizamine [**19**] has a free secondary hydroxyl group at C-14, this example demonstrates the attack of OsO_4 at the nitrogen lone pair in preference to a hydroxyl group. In



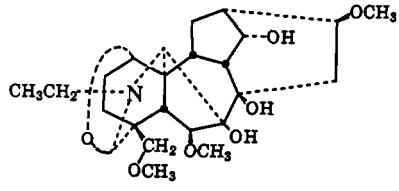
7 R^1=Me, R^2=H_2
9 R^1=CHO, R^2=H_2
10 R^1=Me, R^2=O



13 R^1=Me, R^2=H_2
14 R^1=Me, R^2=O
15 R^1=OH, R^2=H_2
16 R^1=Ac, R^2=H_2
17 R^1=Ac, R^2=O



19 R^1=OH, R^2=H_2
20 R^1=OH, R^2=O
21 R^1=R^2=O



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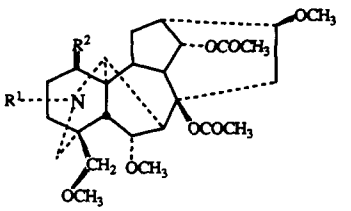
contrast, the reaction of talatizamine [**19**] with chromium trioxide affords 14-dehydro-β-oxotolatizamine [**21**] (7).

Reaction of delphisine [**22**] with 2.5 equivalents of OsO_4 for 30 h afforded *N*-acetyl-*N*-deethyl-1-dehydrodelphisine [**24**] (45.5%) as an amorphous compound. Its structure was derived from its physical and the spectroscopic data. The mass spectrum gave a molecular ion peak at *m/z* 533 $[M]^+$ for $C_{28}H_{39}NO_9$. The ir spectra showed the absence of an OH group and showed an ester carbonyl at 1730 cm^{-1} and an amide carbonyl at 1642 cm^{-1}. In the ^{1}H-nmr spectrum compound **24** showed an additional 3H singlet at δ 2.13 ppm besides the signals at δ 1.94 and 2.01 ppm for the two acetates of delphisine [**22**] and the absence of a peak at δ 1.12 ppm for the methyl of the *N*-CH_2CH_3 group present in delphisine [**22**]. The presence of an *N*-Ac group is also supported by the neutral nature of the product **24** and by its ^{13}C-nmr spectrum, which shows the presence of three acetate groups (170.8, 169.8, 169.5, 22.7, 22.4, and 21.2). The carbonyl singlet at 210.3 ppm is assigned to C-1 on the basis of that reported (5) for 1-dehydrodelphisine (at 212.7 ppm). The presence of a carbonyl group at C-1 is further supported by a singlet at 60.1 ppm for C-11 due to the β effect of a carbonyl group as in the case of 1-dehydrodelphisine (5). The ^{13}C-nmr spectral chemical shifts assignments (Table 1) were made on the basis of a DEPT study. In this reaction 50% of the starting material, delphisine [**22**], was recovered. Interestingly, $KMnO_4$ oxidation of delphisine [**22**] gave two products, *N*-deethyldelphisine and *N*-deethyldelstaphidine (8).

Reaction of 1-*epi*-delphisine [**23**] with 2.5 equivalents of OsO_4 for 24 h afforded *N*-acetyl-*N*-deethyl-1-*epi*-delphisine [**25**] (39.2%) as an amorphous solid. The structure **25** is supported by its physical and spectroscopic data. Its ir spectrum showed the presence of an OH group at 3450 cm^{-1} and an amide carbonyl at 1623 cm^{-1}. The ^{13}C-nmr (Table 1) and the ^{1}H-nmr spectra showed the presence of an additional acetate group



22 R^1=Et, R^2= 

23 R^1=Et, R^2= 

24 R^1=Ac, R^2=O

25 R^1=Ac, R^2= 

(169.9, 22.7, and 2.06 ppm) and absence of an *N*-Et group in the molecule. The presence of an *N*-Ac group is further supported by the presence of the strong signal for an amide carbonyl (1623 cm^{-1}) in the ir spectrum and the fact that the compound was isolated as a neutral product. The molecular formula $C_{28}H_{41}NO_9$ (mol wt 535) for **25** is indicated by a molecular ion peak at *m/z* 535.4 $[M]^+$.

The above results indicate that OsO_4 is a mild, selective oxidizing agent for norditerpenoid alkaloids. This oxidation is of diagnostic value in determining the configuration of the C-6 oxygenated functional group. Thus oxidation of lycoctonine-type alkaloids, bearing a 6β-methoxyl, occurs on the C-19 methylene group to afford a lactam. By contrast, oxidation of aconitine-type alkaloids, bearing a 6α-methoxyl, proceeds with attack on the *N*-alkyl group to furnish an *N*-acyl derivative. An examination of models shows that a C-6 α substituent sterically hinders the C-19 methylene from attack by OsO_4 and thus prevents formation of the C-19 lactam but favors attack on the *N*-alkyl group. In contrast, a C-6 β substituent does not interfere with the C-19 methylene which is then oxidized to a lactam. $KMnO_4$ does not oxidize mesaconitine [**6**] at room temperature (3) and its reaction with delphinine [**7**] results in two products **9** and **10** (4). Oxidation of norditerpenoid alkaloids with OsO_4 gives higher yields of products than with $KMnO_4$.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are corrected and were determined on a Thomas-Kofler hot stage equipped with a microscope and a polarizer. Optical rotations were measured on a Perkin-Elmer model 141 polarimeter. Ir spectra were recorded on a Perkin-Elmer model 1420 spectrophotometer. ^{1}H-nmr spectra were recorded on a JEOL FX-90Q spectrometer in $CDCl_3$ solution with TMS as an internal reference. ^{13}C-nmr spectra were recorded on JEOL FX-60 and FX-90Q spectrometers in $CDCl_3$, and the chemical shifts assignments for several compounds are reported in Table 1. Mass spectra were recorded on a Finnegan Quadrupole 4023 mass spectrometer.

GENERAL PROCEDURE FOR OsO_4 OXIDATION REACTIONS.—The substrate was dissolved in pyridine and then treated with a solution of OsO_4 in *p*-dioxane. The mixture was stirred at room temperature until the starting material disappeared (tlc). A solution of $NaHSO_3$ (200–500 mg) in H_2O and pyridine was then added and stirred for 1 or 2 h. The mixture was then extracted repeatedly with CH_2Cl_2; the extract was washed with H_2O, dried (anhydrous Na_2SO_4), and evaporated in vacuo. The residue was dissolved in $CHCl_3$ (50–60 ml), and the solution was extracted with 1.5% H_2SO_4 (3 ml × 3). The acidic layer was washed with $CHCl_3$ (10 ml × 3) and then basified (pH 8–10) to liberate the basic reaction products. The combined $CHCl_3$ extract was washed with water, dried (anhydrous Na_2SO_4) and evaporated in vacuo to give the mixture of neutral reaction products. The basic and the neutral products were purified by

fractionation by vacuum liquid chromatography (9) or on a Chromatotron rotor (10,11). The major homogeneous products were then characterized in the usual manner.

OXIDATION OF MESACONITINE [**6**] WITH OsO_4.—Mesaconitine (90.24 mg, 0.145 mmol, mp 204–207°) in pyridine (3 ml) was treated with OsO_4 (47.2 mg, 0.185 mmol) in *p*-dioxane (2 ml), and the mixture was stirred for 5 h. The neutral product oxonitine [**8**] (85.1 mg, 92.1%) crystallized from CH_2Cl_2/MeOH, mp 280–281°, and was identical (tlc, cotlc, mmp, ir, and ^{13}C-nmr spectra) with an authentic sample. For the ^{13}C-nmr spectrum see Table 1.

OXIDATION OF DELPHININE [**7**] WITH OsO_4.—Delphinine (74.96 mg, 0.125 mmol) in pyridine (2 ml) was treated with OsO_4 (41.31 mg, 0.162 mmol) in *p*-dioxane (3 ml), and the mixture was stirred for 3 h. The neutral product α-oxodelphinine [**9**] (57.8 mg, 75.0%) crystallized from $CHCl_3$/EtOH, mp 216–218°; $[\alpha]^{22}$ −62.1° (*c* = 0.27, EtOH). Mp, mmp, tlc, cotlc, ir, ^{1}H- and ^{13}C-nmr spectra were identical to those of an authentic sample.

OXIDATION OF ACONITINE [**1**] WITH OsO_4.—Aconitine (9) (126.0 mg, 0.195 mmol) in pyridine (4.0 ml) was treated with OsO_4 (114 mg, 0.449 mmol) in *p*-dioxane (4.0 ml), and the mixture was stirred for 3 h. The neutral product **12** (39.0 mg) was purified by passing its $CHCl_3$ solution through small column of Al_2O_3 (neutral, Activity III, 2.0 g). The residue (21.0 mg, 17.4%) crystallized from Me_2CO/hexane, mp 269–271°; ir (Nujol) ν max 1715 (ester), 1640 (amide) cm^{-1}; ^{1}H nmr δ 1.38 (3H, s, $OCOCH_3$), 2.35 (3H, s, $NCOCH_3$), 3.17, 3.25, 3.30, 3.78 (each 3H, s, OCH_3), 4.18 (1H, d, H-14β), 7.42 to 8.11 (aromatic protons); ^{13}C nmr see Table 1. The compound was identified as *N*-acetyl-*N*-deethylaconitine [**12**] (12).

The basic product (50.0 mg, 39.0%) which crystallized from Et_2O/hexane, mp 167–169°, was identified as the known *N*-deethylaconitine [**11**] (3): ^{1}H nmr δ 1.35 (3H, s, $OCOCH_3$), 3.14, 3.28, 3.30, 3.75 (each 3H, s, OCH_3), 4.08 (1H, d), 4.45 (1H, m, H-15β), 4.88 (1H, d, H-14β), 7.48 to 8.15 (aromatic protons); ^{13}C nmr see Table 1.

OXIDATION OF DELTALINE [**13**] WITH OsO_4.—Deltaline (64.0 mg, 0.126 mmol) in pyridine (4.0 ml) was treated with OsO_4 (84.0 mg, 0.268 mmol) in *p*-dioxane (4.0 ml), and the mixture was stirred for 44 h. The neutral product β-oxodeltaline [**14**] (51.0 mg, 77.0%) crystallized from MeOH, mp 275–277°; $[\alpha]^{23}$ −22.0° (*c* = 0.5, EtOH); ms *m/z* $[M]^+$ 521.1 for $C_{27}H_{39}NO_9$; ir (Nujol) ν max 1740 (ester), 1620 (lactam) cm^{-1}; ^{1}H nmr δ 1.14 (3H, t, *J* = 7 Hz, $N\text{-}CH_2CH_3$), 1.20 (3H, s, $4\text{-}CH_3$), 2.08 (3H, s, $OCOCH_3$), 3.18, 3.32, 3.43 (each 3H, s, OCH_3), 4.18 (1H, dd, *J* = 6 Hz, H-14β), 4.91 (2H, s, OCH_2O), 5.40 (1H, d, *J* = 2 Hz, H-6α); ^{13}C nmr see Table 1.

OXIDATION OF 14-ACETYLDICTYOCARPINE [**16**] WITH OsO_4.—14-Acetyldictyocarpine (40.0 mg, 0.0748 mmol) in pyridine (2.0 ml) was treated with OsO_4 (42.0 mg, 0.1645 mmol) in *p*-dioxane (2.0 ml), and the mixture was stirred for 4.0 h. The neutral product 14-acetyl-β-oxodictyocarpine [**17**] (24.0 mg, 60.0%) crystallized from Et_2O/Me_2CO, mp 284–286°; $[\alpha]^{27}D$ −18.0° (*c* = 0.25, MeOH); mass spectrum *m/z* $[M]^+$ 549 for $C_{28}H_{39}NO_{10}$; ir (Nujol) ν max 1730 (ester), 1620 (lactam) cm^{-1}; ^{1}H nmr δ 1.10 (3H, t, *J* = 7 Hz, $N\text{-}CH_2\text{-}CH_3$), 1.20 (3H, s, $4\text{-}CH_3$), 2.08 (6H, s, $OCOCH_3$), 3.26, 3.33 (each 3H, s, OCH_3), 4.91 and 4.98 (each 1H, s, OCH_2O), 5.30 (1H, m, H-14β), 5.41 (1H, m, H-6α); ^{13}C nmr see Table 1.

The basic product (9.0 mg) was identified as unreacted 14-acetyldictyocarpine [**16**].

OXIDATION OF DELCOSINE [**2**] WITH OsO_4.—Delcosine (64.0 mg, 0.140 mmol) in pyridine (4.0 ml) was treated with OsO_4 (90 mg, 0.353 mmol) in *p*-dioxane (4.0 ml), and the mixture was stirred for 8.0 h. The basic product, 18-methoxygadesine [**18**] (34.0 mg, 53.3%), crystallized from C_6H_6: mp 184–185° [lit. (6) mp 180–184°]; $[\alpha]^{24}$ +72.31° (*c* = 0.52, MeOH); ir (Nujol) ν max 895, 995 (C-O) cm^{-1}; ^{1}H nmr δ 1.10 (3H, t, $N\text{-}CH_2CH_3$), 3.30, 3.39, 3.40 (each 3H, s, OCH_3), 3.70 (1H, m, H-1β), 4.13 (1H, t, H-14β), 3.88, 3.95 (each 1H, s, H-6α or H-19); ^{13}C nmr spectral chemical shifts identical with those reported (7) for 18-methoxygadesine [**18**].

OXIDATION OF TALATIZAMINE [**19**] WITH OsO_4.—Talatizamine (64 mg, 0.152 mmol) in pyridine (3.0 ml), was treated with OsO_4 (85.0 mg, 0.33 mmol) in *p*-dioxane (4.0 ml), and the mixture was stirred for 4.0 h. The neutral compound β-oxotalatizamine [**20**] (49.0 mg, 74.0%) crystallized from Me_2CO: mp 199–200°; $[\alpha]^{24}$ −46.6° (*c* = 0.41, $CHCl_3$) [lit. (7), mp 196–198°, $[\alpha]$ −42° (EtOH)]; ir (Nujol) ν max 1635 cm^{-1} (lactam); ^{1}H nmr δ 1.13 (3H, t, $N\text{-}CH_2\text{-}CH_3$), 3.25, 3.35, 3.43 (each 3H, s, OCH_3), 4.15 (1H, t, H-14β); ^{13}C nmr spectral chemical shifts identical with those reported for β-oxotalatizamine [**20**] (7).

OXIDATION OF DELPHISINE [**22**] WITH OsO_4.—Delphisine (273.4 mg, 0.526 mmol) in pyridine (5.0 ml) was treated with OsO_4 (333.5 mg, 1.3 mmol) in *p*-dioxane (3.0 ml), and the mixture was stirred

for 30 h. The basic product (135.3 mg) was identified as unreacted delphisine. The neutral product **24** (64.1 mg, 45.5%) was amorphous: $[\alpha]^{25}$ −50.2° (*c* = 0.295, $CHCl_3$); ms *m/z* $[M]^+$ 533 for $C_{28}H_{39}NO_9$; ir (Nujol) ν max 1730 (ester), 1700 (C=O), 1642 (amide) cm^{-1}; ^1H nmr δ 1.94, 2.01 (each 3H, s, $OCOCH_3$), 2.13 (3H, s, N-$COCH_3$), 3.24, 3.26, 3.29 (each 3H, s, OMe), 3.54 (2H, dd, *J* = 8.5 Hz, 4-CH_2-OMe), 4.01 (1H, dd, J_1 = 1 Hz, J_2 = 7 Hz, H-6β), 4.84 (1H, dd, $J_1 = J_2$ = 4.5 Hz, H-14β); ^{13}C nmr see Table 1.

OXIDATION OF 1-*epi*-DELPHISINE [**23**] WITH OsO_4.—1-*epi*-Delphisine (52.1 mg, 0.1 mmol) in pyridine (2.5 ml) was treated with OsO_4 (63.5 mg, 0.25 mmol) in *p*-dioxane (1.5 ml), and the mixture was stirred for 24 h. The amorphous neutral product **25** (21.0 mg, 39.2%): ms *m/z* $[M]^+$ 535.1; $[\alpha]^{27}$ −46.5° (*c* = 0.217, $CHCl_3$); ir (Nujol) ν max 3450 (OH), 1730 (ester), 1623 (amide); ^1H nmr δ 1.96, 2.04 (each 3H, s, $OCOCH_3$), 2.06 (3H, s, N-$COCH_3$), 3.24, 3.30, 3.34 (each 3H, s, OCH_3), 3.91 (1H, brm, H-1α), 4.07 (1H, d, *J* = 8.0 Hz, H-6β), 4.86 (1H, t, *J* = 4.5 Hz, H-14β); ^{13}C nmr see Table 1.

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