The Pyrodelphonine Chromophore. Crystal Structures of Pyrodelphinine and Delphinine

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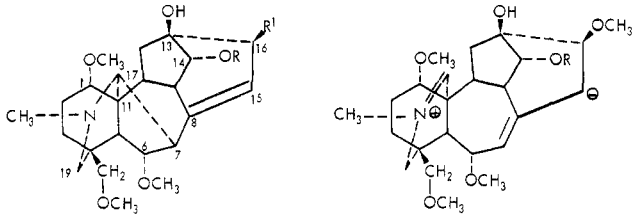
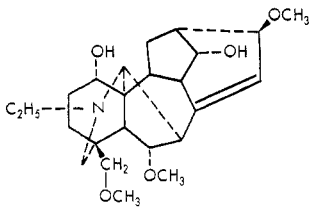
The X-ray crystallographic analysis of pyrodelphinine (**5**) and delphinine (**7**) has established that the resonance structure **6** does not contribute to the structure of pyrodelphinine (**5**) in the electronic ground state. This result suggests that the free electron pair of the nitrogen, the C(7)–C(17) σ bond, and the π electron pair of the C(8)–C(15) double bond of pyrodelphinine are not conjugated in the electronic ground state. The UV absorption spectra of pyrodelphonine, pyroneoline, and α-oxopyrodelphonine are discussed in the terms of the configuration of ring A in these compounds. The position of the double bond and the site of incorporation of deuterium in the photoreduced product obtained from 16-demethoxypyrodelphonine have been established on the basis of chemical and spectral evidence.

In 1960, Wiesner and co-workers[1] reported an unusual UV absorption spectrum displayed by pyrodelphonine [**1**, λ_{max} 245 nm (log ϵ 3.8)] and pyroneoline [**2**, λ_{max} 236 nm (log ϵ 3.85)] which disappears on acidification. They postulated that the free electron pair of the nitrogen, the σ bond [connecting C(7) and C(17)], and the π-electron pair of the double bond are part of an unusual chromophore. They postulated that the excited state of the system may be portrayed as a resonance hybrid between the limiting structures **1** and **3** in pyrodelphonine and similarly in pyroneoline.



1 R = H; R^1 = OCH_3
5 R = Bz; R^1 = OCH_3
4 R = R^1 = H

3 R = H
6 R = Bz



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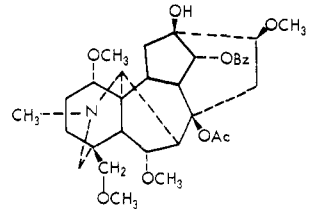

7 Delphinine

Later, Cookson and co-workers[2] presented many examples of a new type of chromophore having the σ-coupled π-electron systems and explained this phenomenon using molecular orbital theory. In 1969, Weisner and Inaba[3] described an unusual photoreduction of the C(17)–C(7) σ bond of 16-dimethoxypyrodelphonine (**4**) by sodium borohydride to support their original views about the nature of chromophoric systems in the excited state of the pyro-derivatives of delphinine and related alkaloids.

Several years ago, a report[4] from this laboratory described studies on the pyrodelphinine (**5**) chromophore in the electronic ground state of the molecule. These results were based on differences in the ^{13}C and ^{1}H NMR spectra of **5** caused by protonation of the nitrogen atom. Thus in the case of pyrodelphinine (**5**) a difference of 30.3 ppm was exhibited between the chemical shift of C(8) (146.6 ppm) and C(15) (116.3 ppm). We pointed out that a difference of 30.3 ppm exhibited by these carbon atoms is higher than that found for the isolated double bonds (10–20 ppm).[5,6] When a double bond is in conjugation with another double bond or keto group, this difference can be as high as 40 ppm. On the basis of these observations, we postulated that the free electron pair of the nitrogen, the C(17)–C(7) σ bond, and the π-electron pair of C(8)–C(15) double bond in **5** are conjugated in the electronic ground state of the molecule, and pyrodelphinine may be portrayed as a resonance hybrid between the limiting structures **5** and **6**. In support of this observation, we pointed out that once the free electron pair on the nitrogen is blocked (as in the case of pyrodelphinine *N*-oxide), the existence of the mesomeric species **6** is not possible and as a result the chemical shift difference between C(8) (142.4 ppm) and C(15) (120.6 ppm) decreases to 21.8 ppm in comparison with **5**. Thus, we concluded that no UV–visible irradiation was necessary for the establishment of **5** ↔ **6**. If this is indeed the case, then pyrodelphinine can be represented as a resonance hybrid between structures **5** and **6** in the electronic ground state.

In this paper, we have reinvestigated the photolytic reduction of 16-demethoxypyrodelphonine (**4**) and established conclusively the position of the double bond and deuterium incorporation in the photoreduced product on the basis of ^{13}C NMR spectral data and chemical evidence. The latter was necessary because the double bond position in the reduced product was based only on the ^{1}H NMR data. Since it would be difficult to differentiate between the double bond at C(7)–C(8) and C(8)–C(15), this problem was investigated by using ^{13}C NMR spectroscopy. We have also studied the UV spectra of pyrodelphonine (**1**), pyroneoline (**2**), and α-oxopyrodelphonine (**18**). Finally, a detailed examination of pyrodelphinine geometry was carried out by comparison of the crystal structure of py-

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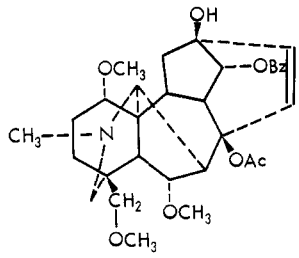
Table I. ^{13}C NMR Shifts and Assignments for Derivatives of Delphinine

	chemical shift, ppm								
carbon	4	5	7	8	9	10	14	15	16
1	86.5	86.1	84.9	85.2	86.6	86.5	89.8	89.9	89.8
2	25.3	25.3	26.3	26.3	26.1	25.3	26.0	26.2	26.0
3	35.3	35.3	34.7	35.0	34.8	35.3	36.2	36.4	36.2
4	39.9	40.0	39.3	39.6	39.4	39.9	40.2	40.3	40.2
5	49.6	48.5	48.8	48.9	48.9	49.9	46.0	46.1	45.9
6	86.0	83.6	83.0	82.2	83.2	84.1	81.3	81.4	81.2
7	50.4	40.4	48.2	44.6	48.1	50.3	126.7	126.9	126.7
8	142.5	146.6	85.4	83.7	85.1	142.0	136.7	136.8	136.7
9	48.3	47.6	45.1	44.3	46.0	46.7	45.1	45.2	45.0
10	46.6	46.7	41.0	42.5	42.4	46.5	43.7	43.8	43.7
11	52.1	51.9	50.2	50.1	50.4	52.3	43.5	43.5	43.4
12	37.2	38.4	35.7	39.2	37.7	38.5	37.5	37.7	37.4
13	76.7	77.7	74.8	76.1	74.9	76.6	77.7	77.8	77.8
14	77.4	79.1	78.9	78.2	79.1	79.7	80.0	80.1	80.0
15	117.5	116.3	39.3	137.3	34.4	117.8	29.7	29.8	
16	39.3	83.6	83.7	125.5	34.8	40.1	40.8	40.7	40.7
17	78.7	78.6	63.3	64.4	63.5	78.6	54.1		
18	80.3	80.3	80.2	80.5	80.4	80.4	80.3	80.4	80.3
19	56.6	56.5	56.1	56.1	56.1	56.7	59.4	59.5	59.4
NCH_3	42.7	42.7	42.3	42.2	41.8	42.8	41.4	41.6	41.4
1′	56.6	56.5	56.1	56.4	56.4	56.7	56.5	56.6	56.5
6′	58.0	58.1	57.6	57.3	57.6	58.1	57.4	57.5	57.4
16′		57.1	58.6						
18′	59.2	59.2	58.9	59.2	59.1	59.3	59.0	59.1	59.0
C=O			169.4	169.6	169.8				
CH_3			21.4	21.8	21.9				
C=O		168.0	166.0	166.9	166.5	167.7			
C_6H_5		130.5	130.4	130.1	130.1	130.1			
		129.6	129.7	129.5	129.9				
		128.1	128.4	128.4	128.5	128.4			
		132.7	132.8	133.2	133.2	133.2			

rodelphinine (5) with that of delphinine (7).

16-Demethoxypyrodelphonine (4) was prepared from delphinine (7) by a series of reactions. Pyrolysis of delphinine (7) afforded mainly pyrodelphinine (5), which on treatment with acetic acid and *p*-toluenesulfonic acid gave the isomerized product, isopyrodelphinine (8). Catalytic



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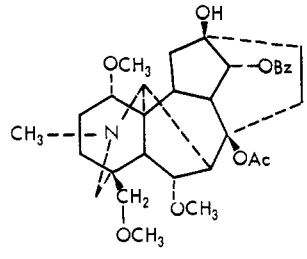

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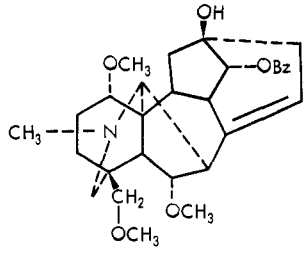

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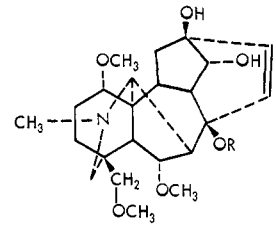
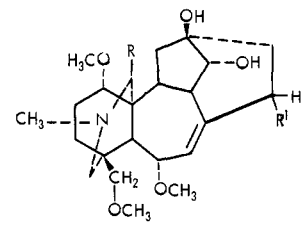
hydrogenation of compound 8 yielded 16-demethoxydelphinine (9). The latter was pyrolyzed to give 16-demethoxypyrodelphinine (10), which on hydrolysis with aqueous KOH afforded the desired compound 4. The structures of these compounds were confirmed by their ^{13}C NMR analysis (Table I). Photoreduction of compound 4 was carried out by using (A) $NaBH_4$/MeOH, (B) $NaBD_4$/MeOH, and (C) $NaBD_4$/MeOD. In all the three cases, the structure of the photoreduced product was established by using ^1H and ^{13}C NMR data.

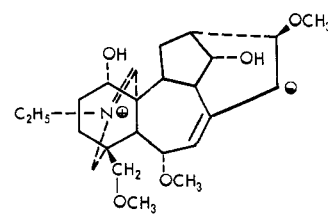
We used 16-demethoxypyrodelphonine [photoreduction of 16-demethoxypyrodelphinine (10) did not occur, probably because the benzoyl group absorbs irradiation in the 254-nm region] instead of pyrodelphonine (1) in the photoreduction because an allylic rearrangement occurs when C(16) is substituted by an alkoxy group. Thus, irradiation of a solution of 1 in methanol containing $NaBH_4$ gave 11.



11 R = CH_3
12 R = CH_2CH_3
13 R = $CH(CH_3)_2$



14 R = R^1 = H
15 R = D; R^1 = H
16 R = R^1 = D



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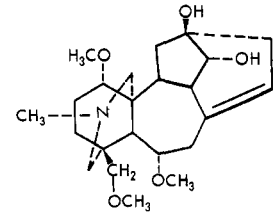


14A

When the same reduction was carried out with ethanol and 2-propanol, the products 12 and 13 were obtained, re-

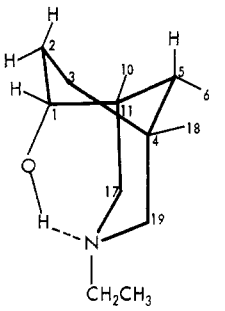
spectively. Wiesner and co-workers[7,8] have observed a similar rearrangement when **5** is treated with acid.

Photoreduction of **4** by using a quartz mercury vapor lamp in the presence of $NaBH_4$/MeOH afforded compound **14**, in which cleavage of the C(17)–C(7) σ bond and isomerization of the C(8)–C(15) double bond were observed in comparison with compound **4**. The two low-field resonances at 136.7 (singlet) and 126.7 ppm (doublet) in the ^{13}C NMR spectrum of the photoreduction product **14** are assigned to C(8) and C(7), respectively (Table I). The alternate structure (**14A**) for the reduced product having the double bond at C(8)–C(15) was considered less likely because in such a compound, the resonance for the C(7) methylene carbon would have appeared at about 35–40 ppm [additive effect of C(6) OMe]. The triplet at 29.7 ppm was ascribed to C(15), while the resonance for C(16) occurs at 40.8 ppm. The resonances for C(9), C(10), and C(6) show small upfield shifts possibly due to the conformational change in the ring B and C of **14**. The singlet at 43.5 ppm is assigned to C(11). There is a significant upfield shift for this carbon in comparison with that in **4**, probably due to the conformational change arising as a result of five-membered-ring cleavage. The two triplets at 54.1 and 59.4 ppm in **14** are assigned to C(17 and C(19), respectively. For confirmation the assignments of C(15) and C(17) in **14**, photoreduction of **4** was carried out by using $NaBD_4$/MeOH. In the photoreduced product **15** the signal at 54.1 ppm in comparison with **14** collapses as a result of the incorporation of the deuterium atom at C(17). Thus in **14**, the signal at 54.1 ppm is assigned to C(17). The other triplet at 59.4 ppm in **14** must then be assigned to C(19). In compound **16**, the product of the photoreduction on using $NaBD_4$/MeOD, the resonances at 54.1 and 29.7 ppm in comparison with those of compound **14** collapse. Thus this finding confirms the assigned resonance at 29.7 ppm to C(15) in **14**. Finally, the structure of the photoreduction product **14** was confirmed by comparison with the C(7)–C(17) seco compound obtained from lithium tri-*tert*-butoxyaluminum hydride reduction[9] of 16-demethoxydelphinine (**9**). They were identical.

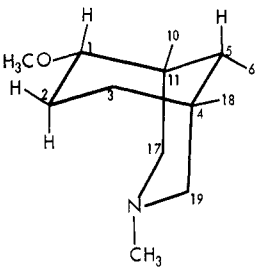
The above data confirm that the double bond in the photoreduced product **14** is indeed between C(7) and C(8), and the structure proposed by Wiesner and Inaba[3] is correct.

We mentioned previously that pyrodelphonine (**1**) shows UV absorption at λ_{max} 245 nm (log ϵ 3.8), whereas pyroneoline (**2**) displays the absorption at λ_{max} 236 nm (log ϵ 3.85). Thus, there is a difference of 9 nm between the λ_{max} of these two compounds. The main differences between pyrodelphonine and pyroneoline are that in the latter, C(1) is substituted by a hydroxyl group, C(13) is unsubstituted, and there is an *N*-ethyl group present instead of an *N*-methyl group.

We have rationalized the difference in the UV absorption between pyrodelphonine and pyroneoline in terms of the availability of the electron pair of the nitrogen for the formation of the resonance species **3** and **17** for pyrodelphonine and pyroneoline, respectively. In the case of pyroneoline, ring A bearing the C(1) α-hydroxy substituent is in a boat conformation (**2A**)[10] in contrast to the chair



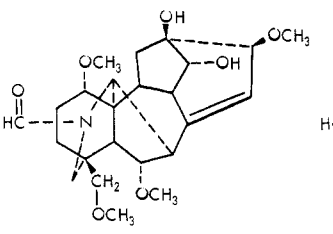
2A



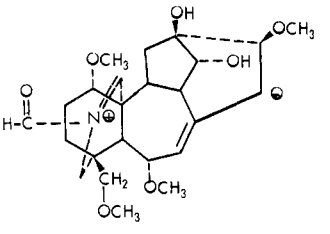
1A

conformation (**1A**) in pyrodelphonine, where the C(1) α substituent is a methoxyl group. The boat conformation of the ring A in pyroneoline is stabilized by the intramolecular hydrogen bonding between the C(1) α-OH group and an electron pair of the nitrogen. Thus, the availability of the electron pair of the nitrogen for the formation of the resonance species **17** is diminished in pyroneoline as compared with pyrodelphonine where there is no possibility of intramolecular hydrogen bonding. This situation explains the difference between the UV absorption of pyrodelphonine and pyroneoline.

To rationalize further, we examined the UV absorption spectrum of α-oxopyrodelphonine (**18**), in which the



18



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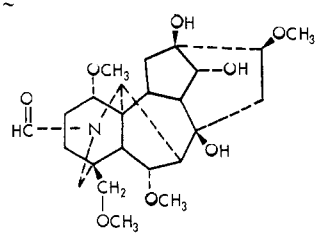

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electron pair of the nitrogen is involved in resonance with the formyl group and hence is not completely available for the formation of resonance structure **18** ↔ **19**. α-Oxopyrodelphonine (**18**) was prepared from the known α-oxopyrodelphinine[8] by alkaline hydrolysis. Compound **18** shows UV absorption at λ_{max} 225 nm (log ϵ 3.83). This absorption is too high for the formyl chromophore responsible for the UV absorption. To determine the UV absorption of the formyl group in the absence of the double bond at C(8)–C(15), we prepared compound **20** by hydrolyzing α-oxodelphinine.[8] Compound **20** shows λ_{max} at 215 nm (log ϵ 3.68), indicating that there is a bathochromic shift of 10 nm in **18** upon the introduction of the double bond at C(8)C(15). Thus, we conclude that the maxima observed in the UV spectra of the pyroderivatives depends on the availability of the free electron pair of the nitrogen.

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Table II. Crystal Data and Data Collection Parameters

parameter	pyrodelphinine (5)	delphinine (7)
mol. formula	$C_{31}H_{41}NO_7$	$C_{33}H_{45}NO_9$
space group	$P2_1$	$P2_12_12_1$
cell constants		
a, Å	12.415 (1)	12.361 (10)
b, Å	8.680 (1)	15.784 (9)
c, Å	13.617 (1)	16.073 (6)
β, deg	104.143 (9)	
V, Å^3	1422.91 (3)	3135.9 (2)
Z	2	4
d_{calcd}, g cm^{-3}	1.26	1.27
d_{measd}, g cm^{-3}	1.29	1.29
radiation	Cu Kα (λ = 1.5418 Å)	Mo Kα (λ = 0.710 69 Å)
μ, cm^{-1}	7.28	0.99
scan technique	$\omega - 2\theta$	$\omega - 2\theta$
scan width, deg	0.95 + 0.142 tan θ	1.15 + 0.35 tan θ
max scan time/ refln, s	120	180
max θ, deg	60	25
cutoff for obsd reflns	$3\sigma(F)$	$2\sigma(F)$
measd reflns	2248	3110
obsd reflns	1930	1408

To decide whether pyrodelphinine is a resonance hybrid of forms **5** and **6** in the electronic ground state, we compared by X-ray analysis (see tables II and III) the detailed geometry of pyrodelphinine with the parent compound, delphinine. The crystal structure of pyrodelphinine confirmed the chemical connectivity and stereochemistry assigned to this compound on the basis of chemical work.[14] To decide whether pyrodelphinine is a resonance hybrid of forms **5** and **6**, a detailed examination of its geometry was necessary. We anticipated that, if **6** represents a significant resonance form of pyrodelphinine, several bond distances and angles would differ from the values expected if **5** alone describes the structure. Bonds C(17)–N and C(7)–C(8) would have some double bond character, and their distances would be unusually short for single bonds. Bonds N–C(19), C(17)–C(11), and C(6)–C(7) might also be expected to be slightly shorter than normal. The C(7)–C(17) and C(8)–C(15) bonds, on the other hand, would be longer than expected. Also, the group of atoms N, C(17), C(19), and C(20) would probably be more nearly planer than normal.

The bond lengths in a structure represented by **5** would be affected by ring strain and substitution pattern. Delphinine is a compound with the same ring system as pyrodelphinine and, except at C(8), has the same pattern of substitution. Furthermore, without a double bond at C(8), a resonance form such as **6** is not possible for this compound. Therefore, the degree to which pyrodelphinine's bond distances and angles, excluding those involving C(8) and C(15), matched those of delphinine would be a measure of the adequacy of **5** as a representation of the structure of pyrodelphinine.

The similarity of delphinine to pyrodelphinine may be noted by a comparison of the perspective drawings of the two molecules (Figure 1 and 2).[15] Rings A, C, E, and F have the same conformations in both molecules. The differences between the two molecules in the conformations of rings B and D can be attributed to the effect of the C(8)–C(15) double bond in pyrodelphinine. The D ring

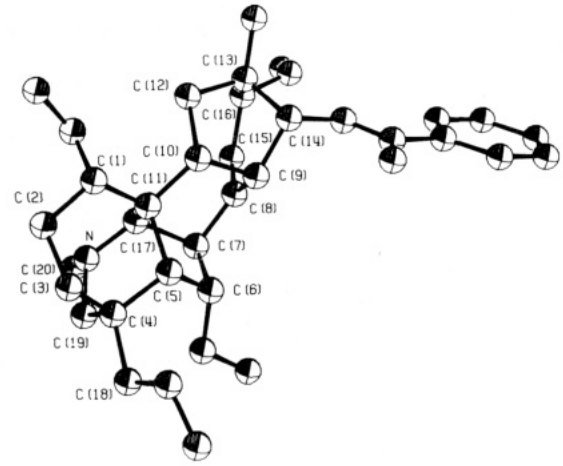

Figure 1. ORTEP drawing of pyrodelphinine (**5**).

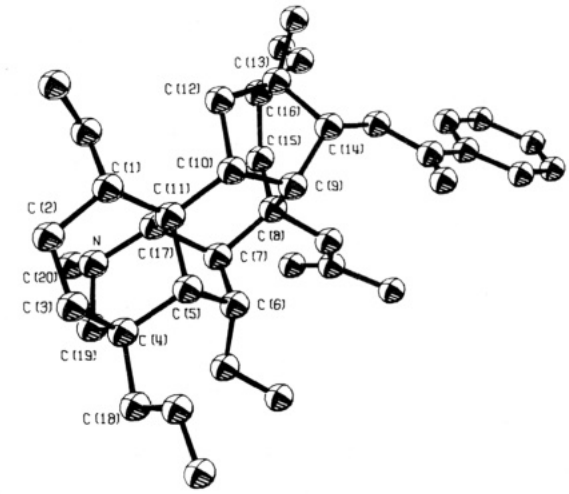

Figure 2. ORTEP drawing of delphinine (**7**).

of delphinine is in a bent-chair conformation with atoms C(8), C(9), C(13), C(15), and C(16) nearly coplanar and C(14) forming the flap. In pyrodelphinine ring D has a half-chair conformation, flattened at the double bond end. The strain in this ring is evident from the large deviation of the double bond system from planarity. The standard deviation for the best plane through atoms C(7), C(8), C(9), C(15), and C(16) is 0.19 Å, while the standard deviation for the best plane through atoms C(7), C(8), C(9), and C(15) is 0.09 Å and the distance of C(16) from this second plane is 0.61 Å.

Tables IV and V list bond distances and angles for both structures. The standard deviations for the molecular parameters of delpohinine are higher than for those of pyrodelphinine since less observed data was available for the former compound. The bond C(8)–C(15) in pyrodelphinine has a typical double bond length of 1.332 (4) Å.[16] The adjacent bonds, as expected, are shortened from an average single bond length, all by approximately the same amount. The value of 1.511 (4) Å for C(7)–C(8) is not unusually short and does not indicate significant double bond character. The C(7)–C(17) bond length of 1.576 (3) Å is long, but is not significantly different[17] from the corresponding bond length in delphinine, 1.563 (9) Å. Similarly, the N–C(17) bond length of 1.455 (4) Å is in good agreement with the corresponding bond length in delphinine, 1.463 (9) Å. The bond angles around the nitrogen

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(15) Johnson, C. K. "ORTEP-II"; Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1971.

(16) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, 1962; Vol. III, p 276.

(17) Cruickshank, D. W. J.; Robertson, A. P. *Acta Crystallogr.* **1953**, *6*, 698.

Table III. Fractional Coordinates of Delphinine and Pyrodelphinine[a]

atom	x	y	z	atom	x	y	z
	(A) Delphinine				(B) Pyrodelphinine		
C(1)	−0.0125 (5)	0.8005 (4)	0.4096 (5)	C(1)	−0.1708 (3)	0.0535 (0)	−0.0947 (2)
C(2)	0.1031 (7)	0.8330 (6)	0.4151 (6)	C(2)	−0.2323 (3)	−0.1396 (4)	−0.0277 (2)
C(3)	0.1829 (7)	0.7674 (6)	0.3856 (5)	C(3)	−0.3216 (3)	−0.2405 (4)	−0.0916 (3)
C(4)	0.1575 (5)	0.7387 (5)	0.2953 (4)	C(4)	−0.4031 (3)	−0.1483 (4)	−0.1729 (2)
C(5)	0.0484 (5)	0.6935 (4)	0.2957 (4)	C(5)	−0.3410 (2)	−0.0858 (4)	−0.2515 (2)
C(6)	0.0067 (5)	0.6696 (5)	0.2061 (4)	C(6)	−0.4124 (2)	0.0254 (4)	−0.3317 (2)
C(7)	−0.0729 (5)	0.7408 (4)	0.1825 (4)	C(7)	−0.3722 (2)	0.1883 (4)	−0.2964 (2)
C(8)	−0.1897 (6)	0.7071 (4)	0.1866 (4)	C(8)	−0.2820 (2)	0.2464 (3)	−0.3440 (2)
C(9)	−0.2028 (6)	0.6585 (5)	0.2695 (4)	C(9)	−0.2106 (2)	0.1161 (3)	−0.3668 (2)
C(10)	−0.1527 (6)	0.7079 (5)	0.3428 (4)	C(10)	−0.1575 (2)	0.0549 (3)	−0.2599 (2)
C(11)	−0.0431 (5)	0.7547 (4)	0.3281 (4)	C(11)	−0.2409 (2)	0.0175 (3)	−0.1936 (2)
C(12)	−0.2496 (6)	0.7652 (5)	0.3704 (5)	C(12)	−0.0669 (2)	0.1823 (3)	−0.2225 (2)
C(13)	−0.3494 (5)	0.7375 (4)	0.3207 (4)	C(13)	−0.0563 (2)	0.2785 (3)	−0.3160 (2)
C(14)	−0.3177 (6)	0.6481 (5)	0.2953 (5)	C(14)	−0.1094 (2)	0.1685 (3)	−0.4008 (2)
C(15)	−0.2780 (6)	0.7720 (5)	0.1723 (5)	C(15)	−0.2444 (2)	0.3906 (3)	−0.3308 (2)
C(16)	−0.3598 (6)	0.7931 (5)	0.2430 (4)	C(16)	−0.1250 (2)	0.4276 (3)	−0.3250 (2)
C(17)	−0.0520 (6)	0.8103 (4)	0.2498 (4)	C(17)	−0.3110 (2)	0.1602 (4)	−0.1820 (2)
C(18)	0.2541 (7)	0.6807 (5)	0.2698 (6)	C(18)	−0.5003 (3)	−0.2557 (5)	−0.2202 (3)
C(19)	0.1485 (6)	0.8131 (5)	0.2342 (5)	C(19)	−0.4517 (3)	−0.0092 (4)	−0.1268 (2)
C(20)	0.0388 (9)	0.9234 (6)	0.1756 (6)	C(20)	−0.4411 (3)	0.2632 (5)	−0.0921 (3)
N	0.0470 (5)	0.8601 (3)	0.2401 (3)	N	−0.3795 (2)	0.1294 (3)	−0.1115 (2)
O(1)	−0.0838 (4)	0.8711 (3)	0.4206 (3)	O(1)	−0.1054 (2)	0.0681 (3)	−0.0400 (1)
C(1A)	−0.0984 (10)	0.8940 (9)	0.5049 (6)	C(1A)	−0.0119 (3)	0.0160 (6)	0.0336 (3)
O(6)	0.0926 (4)	0.6615 (3)	0.1466 (3)	O(6)	−0.5297 (2)	0.0093 (4)	−0.3417 (2)
C(6A)	0.0877 (11)	0.5936 (12)	0.0955 (11)	C(6A)	−0.5949 (3)	0.0744 (10)	−0.4311 (3)
O(8A)	−0.2020 (4)	0.6385 (3)	0.1246 (3)	O(13)	0.0570 (1)	0.3099 (3)	−0.3084 (1)
C(8A)	−0.1990 (7)	0.6533 (6)	0.0420 (5)	O(14A)	−0.1337 (2)	0.2447 (2)	−0.4984 (1)
O(8B)	−0.1855 (5)	0.7210 (4)	0.0109 (3)	C(14A)	−0.1522 (2)	0.1548 (4)	−0.5807 (2)
C(8B)	−0.2180 (11)	0.5723 (7)	−0.0047 (6)	O(14B)	−0.1547 (2)	0.0155 (3)	−0.5762 (1)
O(13)	−0.4441 (4)	0.7406 (4)	0.3687 (3)	C(14B)	−0.1726 (2)	0.2468 (4)	−0.6748 (2)
O(14A)	−0.3911 (4)	0.6206 (3)	0.2300 (3)	C(14C)	−0.1914 (3)	0.1698 (4)	−0.7680 (2)
C(14A)	−0.3884 (6)	0.5389 (4)	0.2040 (5)	C(14D)	−0.2134 (3)	0.2533 (5)	−0.8571 (2)
O(14B)	−0.3312 (5)	0.4873 (3)	0.2368 (4)	C(14E)	−0.2166 (3)	0.4123 (5)	−0.8541 (3)
C(14B)	−0.4610 (5)	0.5250 (4)	0.1339 (4)	C(14F)	−0.1978 (3)	0.4897 (4)	−0.7627 (3)
C(14C)	−0.4723 (7)	0.4432 (5)	0.1037 (6)	C(14G)	−0.1747 (3)	0.4060 (4)	−0.6731 (2)
C(14D)	−0.5443 (10)	0.4290 (8)	0.0389 (7)	O(16)	−0.1020 (2)	0.5208 (2)	−0.4046 (1)
C(14E)	−0.6028 (8)	0.4921 (6)	0.0032 (6)	C(16A)	−0.1283 (3)	0.6784 (4)	−0.3973 (3)
C(14F)	−0.5915 (8)	0.5726 (6)	0.0344 (6)	O(18)	−0.4665 (2)	−0.3685 (3)	−0.2814 (2)
C(14G)	−0.5235 (7)	0.5895 (5)	0.0992 (5)	C(18A)	−0.5571 (3)	−0.4430 (5)	−0.3452 (3)
O(16)	−0.4674 (4)	0.7830 (3)	0.2128 (3)				
C(16A)	−0.5088 (9)	0.8468 (8)	0.1625 (8)				
O(18)	0.2482 (5)	0.6053 (4)	0.3172 (4)				
C(18A)	0.3207 (11)	0.5458 (8)	0.2908 (8)				

[a] The esd's of the least significant figures are given in parentheses. Hydrogens are assigned the same numbers as the heavy atoms to which they are bonded.

in pyrodelphinine are not abnormal for a tetrahedrally bonded atom and compare well with those in delphinine. On the basis of the results presented above, a significant contribution of resonance form **6** to the structure of pyrodelphinine in the crystalline state seems unlikely.

This result in turn suggests that in the electronic ground state of the molecule the free electron pair of the nitrogen, the C(17)–C(7) σ bond, and the π-electron pair of the C(8)–C(15) double bond are not conjugated. The excitation of the electron pair on nitrogen is indeed essential for the occurrence of resonance form **5** ↔ **6**. The conclusion of the NMR study[4] relating to the behavior of the pyrochromophore is not valid because the spectra were taken in acetic acid. The latter forms a salt with pyrodelphinine in which the free electron pair of the nitrogen is not available for participation in the resonance structure **5** ↔ **6**. The change observed in chemical shifts of pyrodelphinine in acetic acid was thus because of solvent effects and protonation of the nitrogen atom.

Experimental Section

Melting points are corrected and were taken on a Thomas-Kofler hot stage equipped with a microscope and polarizer. Rotations were taken in $CHCl_3$ on A Perkin-Elmer polarimeter, Model 141. Infrared spectra were recorded on a Perkin-Elmer polarimeter, Model 297 spectrophotometer. Proton NMR measurements were taken in $CDCl_3$ on JEOL PFT-100, Varian T-60, and Varian EM-390 spectrometers with Me_4Si as an internal standard. The mass spectra were recorded on a Finnigan quadrupole 4023 spectrometer with a direct-inlet system. The following abbreviations are used to express the multiplicity of the signals: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, and m = multiplet. Carbon-13 NMR spectra were taken at 25.03 MHz with JEOL PFT-100 spectrometer and at 15.03 MHz with a JEOL FX-60 spectrometer. ^{13}C chemical shifts are reported in parts per million downfield from Me_4Si. Spectra of the compounds were determined in $CDCl_3$ solution (which also provided the lock signal). Thin-layer chromatography (TLC) was carried out on Merck aluminum oxide GF-254 (Type E or 60/E), and the compounds were visualized in UV light and by spraying with Dragendorff's reagent. Preparative thick-layer chromatography (PTLC) was carried out on 20 × 20 plates coated with 1-mm-thick layer of Merck aluminum oxide 150 PF-254-366 (Type T), and compounds were visualized in UV light. All the solvent extracts were washed with brine and dried over anhydrous sodium sulfate. All reactions were monitored by TLC.

Pyrolysis of Delphinine. Pyrodelphinine (5). Delphinine (250 mg) was pyrolyzed at 230–240 °C under high vacuum (0.01 mm) for 7 min. The melted mass liberated acetic acid. The resulting resinous mass was crystallized from methanol to give the known compound pyrodelphinine (5): 220 mg; mp 208–212 °C; ^1H NMR δ 2.44 (3 H, s, NCH_3), 3.35 and 3.48 (each 3 H, s,

Table IV. Bond Distances of Delphinine and Pyrodelphinine with the Esd's of the Least Significant Figures Given in Parentheses

bond	delphinine	pyro-delphinine
C(1)-C(2)	1.521 (11)	1.522 (5)
C(1)-C(11)	1.543 (9)	1.542 (3)
C(1)-O(1)	1.431 (8)	1.425 (3)
C(2)-C(3)	1.507 (13)	1.511 (5)
C(3)-C(4)	1.554 (10)	1.531 (4)
C(4)-C(5)	1.526 (9)	1.561 (5)
C(4)-C(18)	1.560 (11)	1.536 (5)
C(4)-C(19)	1.534 (11)	1.550 (5)
C(5)-C(6)	1.576 (9)	1.561 (4)
C(5)-C(11)	1.577 (9)	1.579 (4)
C(6)-C(7)	1.541 (10)	1.537 (5)
C(6)-O(6)	1.433 (8)	1.436 (4)
C(7)-C(8)	1.540 (9)	1.511 (4)
C(7)-C(17)	1.563 (9)	1.576 (3)
C(8)-C(9)	1.546 (9)	1.515 (4)
C(8)-C(15)	1.515 (10)	1.332 (4)
C(8)-O(8A)	1.479 (8)	
C(9)-C(10)	1.542 (10)	1.539 (3)
C(9)-C(14)	1.489 (10)	1.510 (4)
C(10)-C(11)	1.561 (9)	1.565 (4)
C(10)-C(12)	1.565 (11)	1.571 (4)
C(11)-C(17)	1.538 (9)	1.543 (4)
C(12)-C(13)	1.534 (10)	1.554 (4)
C(13)-C(14)	1.520 (10)	1.519 (4)
C(13)-C(16)	1.532 (10)	1.538 (4)
C(13)-O(13)	1.402 (9)	1.412 (3)
C(14)-O(14A)	1.453 (9)	1.449 (3)
C(15)-C(16)	1.557 (10)	1.500 (4)
C(16)-O(16)	1.425 (8)	1.436 (4)
C(17)-N	1.463 (9)	1.455 (4)
C(18)-O(18)	1.415 (11)	1.415 (5)
C(19)-N	1.461 (10)	1.483 (4)
C(20)-N	1.444 (11)	1.450 (5)
O(1)-C(1A)	1.414 (11)	1.410 (4)
O(6)-C(6A)	1.353 (20)	1.404 (5)
O(8A)-C(8A)	1.349 (9)	
C(8A)-O(8B)	1.192 (11)	
C(8A)-C(8B)	1.501 (14)	
O(14A)-C(14A)	1.355 (8)	1.339 (3)
C(14A)-O(14B)	1.200 (9)	1.212 (4)
C(14A)-C(14B)	1.458 (10)	1.477 (4)
C(14B)-C(14C)	1.385 (10)	1.403 (4)
C(14B)-C(14G)	1.395 (10)	1.382 (5)
C(14C)-C(14D)	1.389 (15)	1.381 (5)
C(14D)-C(14E)	1.358 (15)	1.381 (6)
C(14E)-C(14F)	1.374 (14)	1.383 (5)
C(14F)-C(14G)	1.365 (13)	1.389 (4)
O(16)-C(16A)	1.389 (14)	1.416 (4)
O(18)-C(18A)	1.366 (15)	1.400 (4)

OCH_3), 3.40 (6 H, s, 2 OCH_3), 4.06 (1 H, s, C(6) β-H), 5.17 (1 H, d, C(14) β-H), 5.78 (1 H, d, C(15) H), 7.76–8.38 (aromatic protons); ^{13}C NM R, see Table I.

Isomerization of Pyrodelphinine (5) to Isopyrodelphinine (8). A solution of pyrodelphinine (280 mg), *p*-toluenesulfonic acid (150 mg), and acetic acid (20 mL) was stirred at room temperature for 30 minutes, and subsequently the reaction mixture was heated in an oil bath at 70–80 °C for 1 h. The solvent was removed in vacuo, and the residue was diluted with water and made alkaline with 10% aqueous NaOH. Extraction with CH_2Cl_2 (3 × 30 mL) afforded the CH_2Cl_2 extract which was washed with water and brine and dried over anhydrous sodium sulfate. Removal of the solvent gave 200 mg of the residue. The TLC of this residue (Al_2O_3, EtOH–hexane) indicated it to be a mixture of one major compound along with small amounts of polar and nonpolar components. From this mixture, the major compound 8 (146 mg) was obtained by column chromatography over Al_2O_3 (activity III). All attempts to crystallize this compound met with failure: $[\alpha]^{29}_D$ + 23.91° (*c* 0.23, MeOH); IR (Nujol) ν_{max} 3433 (OH), 1720 (>C=O) cm^{-1}; ^1H NMR δ 1.35 (3 H, s, $OCOCH_3$), 3.20, 3.30, and 3.35 (each 3 H, s, OCH_3), 5.01 (1 H, m, C(14) β-H), 6.13 and 6.63 (1 H each, dd, CH=CH, *J* = 10.5 Hz), 7.41, 7.68, 8.08, and 8.18 (aromatic protons); ^{13}C NMR, see Table I; mass spectrum, obsd *m/z* 567, required for $C_{32}H_{41}NO_8$ *m/z* 567.

Hydrogenaton of Compound 8 to 16-Demethoxydelphinine (9). Compound 8 (485 mg) was hydrogenated in 30 mL of glacial acetic acid by using 540 mg of 10% Pd/C catalyst at an ~3.5-atm pressure for 42 h. The usual workup gave a residue (330 mg) which on TLC (Al_2O_3, EtOH–hexane) was found to be a mixture of several compounds. From this mixture, the desired reduced product 9 (242 mg) was obtained by PTLC (Al_2O_3) as an amorphous solid: $[\alpha]^{29}_D$ +18° (*c* 0.17, MeOH); IR ν_{max} (CH_2Cl_2) 3585 (OH), 1720 (>C=O) cm^{-1}; ^1H NMR δ 1.38 (3 H, s, $OCOCH_3$), 2.31 (3 H, s, NCH_3), 3.15 (3 H, s, OCH_3), 3.28 (6 H, s, 2 OCH_3), 4.9 (1 H, d, C(14) β-H), 7.33–8.01 (aromatic protons); ^{13}C NMR, see Table I; mass spectrum, obsd *m/z* 569, required for $C_{32}H_{43}NO_8$ *m/z* 569.

Pyrolysis of 16-Demethoxydelphinine (9) to 16-Demethoxypyrodelphinine (10). 16-Demethoxydelphinine (9, 220 mg) was subjected to pyrolysis at 220–230 °C for 5 min under a 0.01-mm pressure. The resulting resinous mass (210 mg) was purified by PTLC (Al_2O_3, EtOH–hexane) to yield 173 mg of pure 16-demethoxypyrodelphinine: mp 159.2–163.2 °C; $[\alpha]^{24}_D$ +172.25° (*c* 0.31, MeOH); IR ν_{max} (Nujol) 3463 (OH), 1691 (C=O), 1604 (C=C), 1091 (ether) cm^{-1}; ^1H NMR δ 2.36 (3 H, s, NCH_3), 3.21, 3.25, 3.28 (each 3 H, s, OCH_3), 5.00 (1 H, d, C(14) β-H), 5.18 (1 H, dd, C=CH) 7.35–8.01 (aromatic protons); ^{13}C NMR, see Table I; mass spectrum, obsd *m/z* 509, required for $C_{30}H_{39}NO_6$ *m/z* 509.

Hydrolysis of 16-Demethoxypyrodelphinine (10) to 16-Demethoxypyrodelphonine (4). Compound 10 (148 mg) was dissolved in methanol and 1 mL of 5% methanolic KOH. The resulting solution was stirred at room temperature for 9 h. After this time the methanol was evaporated in vacuo, and the aqueous layer was extracted with chloroform. The chloroform layer on evaporation gave 16-demethoxypyrodelphonine (102 mg) as an amorphous solid: $[\alpha]^{24}_D$ +178.69° (*c* 0.23, MeOH); IR ν_{max} (nujol) 3383 (OH), 1640 (C=C) cm^{-1}; ^1H NMR δ 2.35 (3 H, s, NCH_3), 3.25, 3.26, 3.28 (each 3 H, s, OCH_3), 3.83 (1 H, d, C(14) β-H), 5.21 (1 H, dd, C=CH); ^{13}C NMR, see Table I; mass spectrum, obsd *m/z* 405, required for $C_{23}H_{35}NO_5$ *m/z* 405.

Photoreduction of 16-Demethoxypyrodelphonine (4). Method A. In a typical photoreduction experiment, 80 mg of 4 in MeOH (25 mL) was irradiated at 0–5 °C with a quartz mercury vapor lamp in the presence of $NaBH_4$ (80 mg) for 1.5 h. Excess borohydride was decomposed, and methanol was evaporated under vacuum. The residue was diluted with water and extracted with chloroform. Evaporation of solvent under vacuum gave a residue (77 mg) which was found to be a mixture of at least three compounds on TLC (Al_2O_3, EtOH–hexane). The separation of the individual components of the mixture was attempted by using PTLC (Al_2O_3) to give 11 mg of the reduced product 14: IR (Nujol) ν_{max} 3370 (OH), 1095 (ether) cm^{-1}; ^1H NMR δ 2.10 (3 H, s, NCH_3), 3.26 (9 H, br s, OCH_3), 3.90 (1 H, d, C(14) β-H), and 5.36 (1 H, undefined m, C=CH); ^{13}C NMR, see Table I; mass spectrum, obsd *m/z* 407, required for $C_{23}H_{37}NO_5$ *m/z* 407. The other major compound (4, 41 mg) from this chromatography was found to be the starting material.

Method B. In a similar manner, compound 4 (100 mg) in MeOH (30 mL) was irradiated in the presence of $NaBD_4$ (110 mg) at 0–5 °C. The usual workup afforded a mixture (85 mg) from which the desired photoreduced product 15 (14.5 mg) was obtained by PTLC over alumina: ^1H NMR δ 2.13 (3 H, s, NCH_3), 3.36 (9 gh, br s, 3 OCH_3)8 3.98 (1 H, d, C(14) β-H), 5.5 (1 H, m, C=CH); ^{13}C NMR see Table I; mass spectrum, obsd *m/z* 408, required for $C_{23}H_{36}DNO_5$ *m/z* 408.

Method C. The above photoreduction experiment was also carried out by using $NaBD_4$ and MeOD. Thus compound 4 (95 mg) in MeOD was irradiated at 0–5 °C with a quartz Hg vapor lamp in the presence of $NaBD_4$ (100 mg) for 3 h. The usual workup followed by PTLC over alumina gave the desired photoreduced product 16 (27 mg) along with the starting 16-demethoxypyrodelphonine (40.5 mg): ^1H NMR δ 2.10 (3 H, s, NCH_3), 3.30 (9 H, br s, OCH_3), 3.88 (1 H, d, C(14) β-H), 5.37 (1 H, m, C=CH); ^{13}C NMR, see Table I; mass spectrum, obsd *m/z* 409, required for $C_{23}H_{35}D_2NO_5$ *m/z* 409.

Preparation of the 7,17-Seco Compound 14 from 16-Demethoxydelphinine (9). 16-Demethoxydelphinine (350 mg) was dissolved in anhydrous diglyme (13 mL) previously heated to 140 °C, and to this stirred solution was added rapidly freshly prepared

Table V. Bond Angles of Delphinine and Pyrodelphinine with Esd's of the Least Significant Figures Given in Parentheses

angle	delphinine	pyrodelphinine	angle	delphinine	pyrodelphinine
C(2)-C(1)-C(11)	115.9 (6)	117.5 (2)	C(12)-C(13)-C(16)	109.2 (6)	111.2 (2)
C(2)-C(1)-O(1)	108.0 (6)	110.9 (2)	C(12)-C(13)-O(13)	112.0 (6)	109.1 (2)
C(11)-C(1)-O(1)	108.6 (5)	106.7 (1)	C(14)-C(13)-C(16)	109.5 (6)	109.8 (2)
C(1)-C(2)-C(3)	111.5 (7)	110.1 (3)	C(14)-C(13)-O(13)	113.3 (6)	114.6 (2)
C(2)-C(3)-C(4)	111.2 (7)	112.1 (3)	C(16)-C(13)-O(13)	110.9 (5)	111.5 (2)
C(3)-C(4)-C(5)	108.1 (6)	109.1 (3)	C(9)-C(14)-C(13)	102.6 (6)	101.2 (2)
C(3)-C(4)-C(18)	105.1 (6)	107.3 (3)	C(9)-C(14)-O(14A)	115.3 (6)	114.6 (2)
C(3)-C(4)-C(19)	112.9 (6)	111.6 (3)	C(13)-C(14)-O(14A)	108.1 (5)	111.4 (2)
C(5)-C(4)-C(18)	113.8 (6)	113.1 (3)	C(8)-C(15)-C(16)	120.1 (6)	121.2 (3)
C(5)-C(4)-C(19)	107.3 (6)	108.3 (3)	C(13)-C(16)-C(15)	114.7 (6)	110.2 (2)
C(18)-C(4)-C(19)	109.7 (6)	107.4 (3)	C(13)-C(16)-O(16)	107.0 (6)	109.1 (2)
C(4)-C(5)-C(6)	113.4 (5)	113.8 (2)	C(15)-C(16)-O(16)	109.5 (6)	117.2 (2)
C(4)-C(5)-C(11)	110.4 (5)	108.4 (2)	C(7)-C(17)-C(11)	100.2 (5)	99.8 (2)
C(6)-C(5)-C(11)	102.4 (5)	104.0 (2)	C(7)-C(17)-N	116.2 (5)	117.5 (2)
C(5)-C(6)-C(7)	105.0 (5)	105.3 (2)	C(11)-C(17)-N	109.5 (5)	110.8 (2)
C(5)-C(6)-O(6)	112.9 (5)	113.3 (3)	C(4)-C(18)-O(18)	108.2 (7)	110.6 (3)
C(7)-C(6)-O(6)	112.0 (6)	111.3 (3)	C(4)-C(19)-N	114.2 (6)	114.1 (3)
C(6)-C(7)-C(8)	109.7 (5)	113.0 (2)	C(17)-N-C(19)	116.9 (6)	119.1 (2)
C(6)-C(7)-C(17)	103.7 (5)	102.0 (2)	C(17)-N-C(20)	113.0 (6)	113.1 (3)
C(8)-C(7)-C(17)	111.6 (5)	104.3 (2)	C(19)-N-C(20)	111.4 (7)	110.4 (3)
C(7)-C(8)-C(9)	107.8 (5)	111.8 (2)	C(1)-O(1)-C(1A)	113.3 (7)	113.5 (3)
C(7)-C(8)-C(15)	115.8 (6)	121.9 (3)	C(6)-O(6)-C(6A)	116.3 (8)	113.5 (3)
C(7)-C(8)-O(8A)	108.7 (5)		C(8)-O(8A)-C(8A)	122.3 (6)	
C(9)-C(8)-C(15)	113.0 (6)	121.7 (3)	O(8A)-C(8A)-O(8B)	124.9 (8)	
C(9)-C(8)-O(8A)	101.9 (5)		O(8A)-C(8A)-C(8B)	109.9 (7)	
C(15)-C(8)-O(8A)	108.6 (5)		O(8B)-C(8A)-C(8B)	125.2 (7)	
C(8)-C(9)-C(10)	111.4 (6)	101.6 (2)	C(14)-O(14A)-C(14A)	119.5 (5)	117.2 (2)
C(8)-C(9)-C(14)	113.2 (6)	114.2 (2)	O(14A)-C(14A)-O(14B)	121.7 (7)	122.7 (2)
C(10)-C(9)-C(14)	103.1 (6)	101.4 (2)	O(14A)-C(14A)-C(14B)	111.5 (6)	111.7 (3)
C(9)-C(10)-C(11)	118.2 (6)	115.3 (2)	O(14B)-C(14A)-C(14B)	126.8 (6)	125.6 (3)
C(9)-C(10)-C(12)	101.6 (6)	99.8 (2)	C(14A)-C(14B)-C(14C)	118.2 (6)	118.9 (3)
C(11)-C(10)-C(12)	115.7 (6)	118.8 (2)	C(14A)-C(14B)-C(14G)	122.7 (6)	121.7 (3)
C(1)-C(11)-C(5)	113.1 (5)	114.6 (2)	C(14C)-C(14B)-C(14G)	119.0 (7)	119.4 (3)
C(1)-C(11)-C(10)	107.8 (5)	106.0 (2)	C(14B)-C(14C)-C(14D)	118.6 (8)	119.9 (3)
C(1)-C(11)-C(17)	116.4 (5)	116.3 (2)	C(14C)-C(14D)-C(14E)	122.7 (10)	120.0 (3)
C(5)-C(11)-C(10)	112.5 (5)	112.3 (2)	C(14D)-C(14E)-C(14F)	118.0 (9)	120.8 (3)
C(5)-C(11)-C(17)	97.5 (5)	96.4 (2)	C(14E)-C(14F)-C(14G)	121.5 (9)	119.3 (3)
C(10)-C(11)-C(17)	109.3 (5)	111.2 (2)	C(14B)-C(14G)-C(14F)	120.2 (8)	120.6 (3)
C(10)-C(12)-C(13)	107.6 (6)	108.1 (2)	C(16)-O(16)-C(16A)	117.5 (7)	113.6 (3)
C(12)-C(13)-C(14)	101.4 (6)	100.2 (2)	C(18)-O(18)-C(18A)	112.1 (8)	112.1 (3)

lithium tri-*tert*-butoxyaluminum hydride (400 mg) dissolved in diglyme (17 mL previously heated to 100 °C) was added rapidly in a nitrogen atmosphere. The temperature was maintained at 140 °C for 17–20 min, and the mixture was cooled. The excess of reagent was destroyed by the cautious addition of methanol. Celite was added to facilitate filtration, followed by water, and the mixture was filtered through Celite. The filter cake was washed thoroughly with methanol, and the combined filtrate and washings were evaporated in vacuo by using first a water pump and subsequently an oil pump. The residue was dissolved in water, and the solution was extracted with dichloromethane. The gummy residue (310 mg) obtained on evaporation of the dried (anhydrous Na_2SO_4) dichloromethane extract showed mainly two spots on TLC (Al_2O_3; hexane/toluene/diethylamine/ethyl acetate, 4.25:4.25:0.5:1.0). The two products were separated by column chromatography (Al_2O_3, activity III, hexane/ethanol). The major compound (110 mg) was found to be the 7,17-seco compound which was identical (^{13}C and ^1H NMR, MS, and TLC) with the photoreduction product 14.

The minor polar compound (21 mg) was identified as 16-demethoxypyrodelphonine, having identical ^{13}C and ^1H NMR spectra and a TLC R_f value with those of compound 4 reported earlier in this paper.

X-ray Crystal Structure Determinations for Pyrodelphinine (5) and Delphinine (7). Preliminary examination and data collection for both crystals were done on an Enraf-Nonius CAD-4 diffractometer. Experimental data are summarized in Table II. The data were corrected for Lorentz and polarization effects but, because of the small absorption coefficients for the compounds, absorption corrections were not made.

The crystal structure of pyrodelphinine was solved with difficulty by direct methods. MULTAN 76[11] was used to develop phases for the largest 275 E's but the E maps calculated from the possible solutions did not even show a recognizable fragment of the molecule. Part of the problem seemed to be that the *h0l* reflections, which for space group $P2_1$ have phases restricted to 0 or π, were exceptionally strong and dominated the end of the convergence map. Consequently, phases of general reflections were not well-determined. To deal with this problem, the amplitudes of the *h0l* reflections were scaled by 0.70, and the E's were recalculated. So successful was this technique in removing the special reflections from the end of the convergence map that MULTAN was forced to choose three general reflections to define the origin, one of which was allowed two values in the phase-determining process. Five additional reflections were included in the starting set, and a total of 240 possible solutions were generated. An E map calculated from one set showed the benzoyl group of the molecule, and this fragment was elaborated by using the recycling procedure of Karle[12] until 35 of the 39 nonhydrogens were located. The remaining nonhydrogen atoms as well as all hydrogens were located by means of difference syntheses.[13] Heavy atoms were refined anisotropically, and hydrogens were refined isotropically by blocked least-squares methods to $R = 0.039$ and $R_w = 0.043$. The quantity minimized in least-squares calculations was $w(|F_0| - |F_c|)^2$ where $w = (1.0 + ((|F_0| - 6.0)/6.0)^2)^{-1}$. At this point, four reflections with low θ values whose intensities appeared to have been significantly reduced by secondary extinction were excluded from the data set and refinement continued until convergence at $R = 0.036$ and $R_w = 0.042$. The average ratio of parameter shift to error in the final least-squares calculation was 0.11, and the maximum ratio was 1.02. A final difference map showed no peaks greater than 0.14 e Å^{-3}.

The crystal structure of delphinine was also determined by direct methods.[11] A starting set of five reflections was used to generate 120 possible phase sets for the 275 largest E's. The solution with the fourth highest overall figure of merit yielded

an E map showing an 18-atom fragment of the molecule. Several successive Fourier syntheses[13] served to locate the remaining nonhydrogen atoms. Hydrogens were located on difference maps after partial refinement of the nonhydrogen atoms. The latter were refined anisotropically and hydrogens were refined isotropically by using blocked least-squares methods and minimizing the quantity $w(|F_o| - |F_c|)^2$, wherre $w = (1.0 + ((|F_o| - 16.0)/12.0)^2)^{-1}$. Some of the thermal parameters for C(6A) were more than twice as large as those for other atoms in the molecule, but no more than one discrete position for this methyl could be found on difference maps, so a disordered model was not used. The hydrogens attached to C(6A) did not refine to reasonable positions, and so they were fixed in ideal positions with isotropic temperature factors slightly higher than the isotropic temperature factor of C(6A). Refinement was terminated at $R = 0.043$ and $R_w = 0.056$ when the average ratio of parameter shift to error was 0.11 and the maximum ratio was 0.74. A final difference map showed no peaks greater than 0.14 e Å^{-3}.

Registry No. **4**, 83710-13-8; **5**, 60050-12-6; **7**, 561-07-9; **8**, 60450-64-8; **9**, 83705-17-3; **10**, 83705-18-4; **14**, 83705-19-5; **15**, 83705-20-8; **16**, 83705-21-9.

Stereocontrolled Synthesis of Exocyclic Trisubstituted Double Bonds by Stereospecific Iminium Ion–Vinylsilane Cyclizations. A Short Synthetic Route to Indoloquinolizidine Alkaloids[1]

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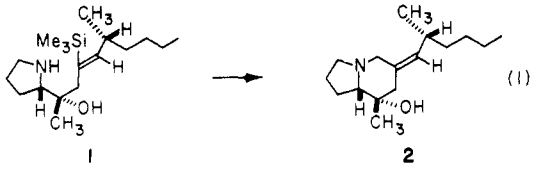
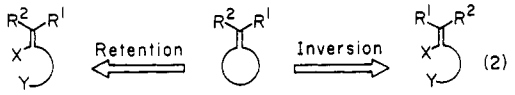
The reaction of (*Z*)- and (*E*)-trisubstituted vinylsilanes **9** and **10** with paraformaldehyde and acid proceeded with >98% retention of configuration to give indoloquinolizidines **13** and **3** in excellent yield. This is the first demonstration that iminium ion–vinylsilane cyclizations occur with complete retention of configuration with either vinylsilane stereoisomer. The simple indole alkaloid *dl*-deplancheine (**3**) was prepared in a stereocontrolled fashion in 26% overall yield from commercially available 1-(trimethylsilyl)propyne.

Significant advances have been made in recent years in stereoselective synthesis of alkenes.[2] In spite of this progress, stereocontrol in the preparation of alkenes which are exocyclic to a ring remains an unsolved problem.[3] We recently reported[1] the stereospecific[4] cyclization of (*Z*)-vinylsilane **1** upon treatment with formaldehyde and acid to form the (*Z*)-alkylideneindolizidine ring of *Dendrobatid* toxin 251D (**2**, eq 1). This is an example of a potentially

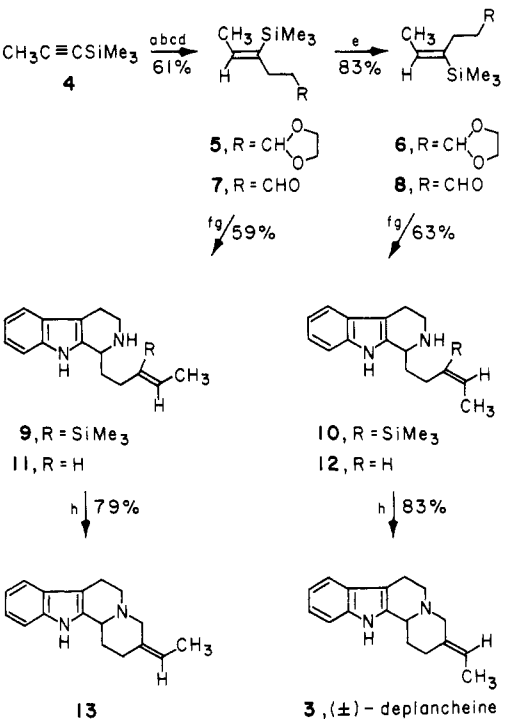


general stereocontrolled approach to exocyclic alkenes (eq 2) in which stereochemistry is established in an acyclic



synthon and then transferred to the desired cyclic product via a stereospecific cyclization reaction which proceeds with either inversion or retention of alkene stereochemistry. Since a variety of methods are available for the stereoselective synthesis of vinylsilanes,[5] iminum ion–vinylsilane

Scheme I[a]



[a] (a) Bu_2AlH, EtO_2, 40 °C; (b) Br_2, pyridine, −78 °C to room temperature; (c) *sec*-BuLi, THF, −78 °C; (d) $ICH_2CH(OCH_2CH_2O)$, −78 °C to room temperature; (e) NBS (catalytic amount), $h\nu$, 0 °C; (f) 0.5 N HCl, THF-H_2O, 25 °C; (g) tryptamine hydrochloride, methanol-H_2O, 85 °C; (h) $(CH_2O)_n$, $CamSO_3H$, CH_3CN, 80 °C.

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