Thebaine Rearrangements: Nonclassical D Ring Migrations

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3,6-Dimethoxy-4-acetoxy-5-[2-(*N*-methylacetamido)ethyl]phenanthrene (**3**) and its isomer 3,6-dimethoxy-4-acetoxy-8-[2-(*N*-methylacetamido)ethyl]phenanthrene (**4**) have been detected as manufacturing byproducts at trace levels in illicit heroin. These compounds are novel rearrangement products obtained by the action of acetic anhydride (Ac_2O) on thebaine (**1**). The syntheses of **3** and **4** from **1** proceed via the intermediate $\Delta^{5,7,9(14)}$-*N*-acetyldesthebaine (**2**). Structural characterization and optimization of synthetic conditions for **3** and **4** are described. A brief discussion is also given concerning other neutral products of **1** obtained under Ac_2O conditions.

Introduction

We, and others, have previously reported on the in-depth analyses of trace levels of manufacturing byproducts in illicit heroin.[1-3] The characterization of these impurities is of importance for forensic purposes, especially in providing evidence of conspiracy. Many of these impurities result from the action of acetic anhydride on morphine and other alkaloids of the opium poppy, Papaver somniferum L. We have recently focused our attention on the action of acetic anhydride upon **1**, a prominent opium alkaloid. Previous studies of this, and other reactions of **1**, have resulted in the characterization of many compounds, including **6**,[5] **7**,[6] **8**,[7] **9**,[8,9] **10**,[4] **11**,[4] and **12**[4] (see Scheme I).

We now report on the unequivocal identification of two additional trace heroin impurities, **3** and **4** (see Scheme I), resulting from the decomposition of **1** in acetic anhydride. Compound **3** is structurally analogous to **12**, as proposed by Bertgen and co-workers.[4] Initially, we were skeptical about the structural assignment of **12** for a number of reasons. First, the migration of the ethylamide chain from C-13 to C-5 is in contrast to all previously published works which show that the C-13 side chain moves to C-14. Secondly, migration to C-5 of the ethylamide chain from C-13 to C-5 would be expected to introduce a high degree of steric crowding in the bay of the phenanthrene structure making this an unfavorable direction of migration. Lastly, the structural assignment of **12** by Bertgen et al.[4] was based primarily upon ultraviolet spectroscopy. However, when we synthesized **12** via the earlier work of Bertgen et al. the ^1H NMR spectrum obtained was consistent with their structure.

As described below and illustrated in Schemes I and II, we propose that the formation of the unusual rearrangement products **3** and **4** from **1** proceeds through the intermediate **2** and the transient species **2a**.

Results and Discussion

The products obtained upon the treatment of **1** with acetic anhydride are illustrated in Table I. Under conditions A, B, and C (Table I), small quantities of **3** and **4** were produced. Addition of lithium chloride (condition D) as a Lewis acid to coordinate the epoxide oxygen improved the yields of **3** and **4** to 30% of total neutral products. The marked effect that lithium chloride has upon the reaction is evident by the absence of **2**, **9**, **10**, and other neutral products and the enhanced yields of **3**, **4**, and **8**. Although the formation of **2** is prominent under conditions A, B, and C, this substance is unstable and is difficult to detect in illicit heroin. The fate of **2** in aged samples is believed to be the elimination of the C-13 side chain to yield **9** and **10**, both detectable in some heroin samples. Both **3** and **4** are stable and can be detected in heroin samples at levels from 0.1% to below 0.001%.

Table I. Products of Thebaine Rearrangements in Acetic Anhydride[a]

	compd, % determined by GC						
conditn[b]	**2**	**3**	**4**	**8**	**9**	**10**	others
A	31	5	4	9	4	24	23
B	26	4	4	15	3	22	26
C	32	6	4	12	3	24	19
D		21	9	70			1

[a] All reactions were done using 100 mg of **1** in Ac_2O at 100 °C for 1 h. [b] Conditions: A, Ac_2O (2 mL); B, Ac_2O (2 mL), HOAc (50 mg); C, Ac_2O (2 mL), NaOAc (50 mg); D, Ac_2O (2 mL), LiCl (50 mg).

The formation of **2** suggests that, prior to the opening of the epoxide in **1**, the D ring is cleaved at the C-9 to N bond. This is in contrast to rearrangements involving morphine, codeine, and thebaine which retain elements of the D ring via the C-9 to N bond, e.g., apomorphine, apocodeine, and morphothebaine.[10] The formation of **2** may be envisioned as the loss of the weakly acidic proton at C-5 in **1** followed by migration of the diene system from $\Delta^{6,8}$ to $\Delta^{7,9(14)}$ with concomitant cleavage of the D ring at C-9 to N. The fate of **2** in acetic anhydride, and the eventual formation of **3** and **4** may proceed through the transient intermediate **2a** (Schemes I and II). The formation of **2a**, which exhibits extended conjugation from ring A through ring C, seems reasonable in that it readily allows the rationalization for the production of **3** and **4**. The proposed mechanism for the formation of **3** is straightforward. The first step is believed to be the opening of the epoxide in **2a**, resulting in a resonance

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(4) Bertgen, C.; Fleischhacker, W.; Viebock, F. *Chem. Ber.* **1967**, *100*, 3002.
(5) (a) Freund, M.; Michaels, H.; Gobel, E. *Chem. Ber.* **1897**, *30*, 1357. See also: (b) Schopf, C.; Bordowsky, F. *Liebigs Ann. Chem.* **1927**, *458*, 148.
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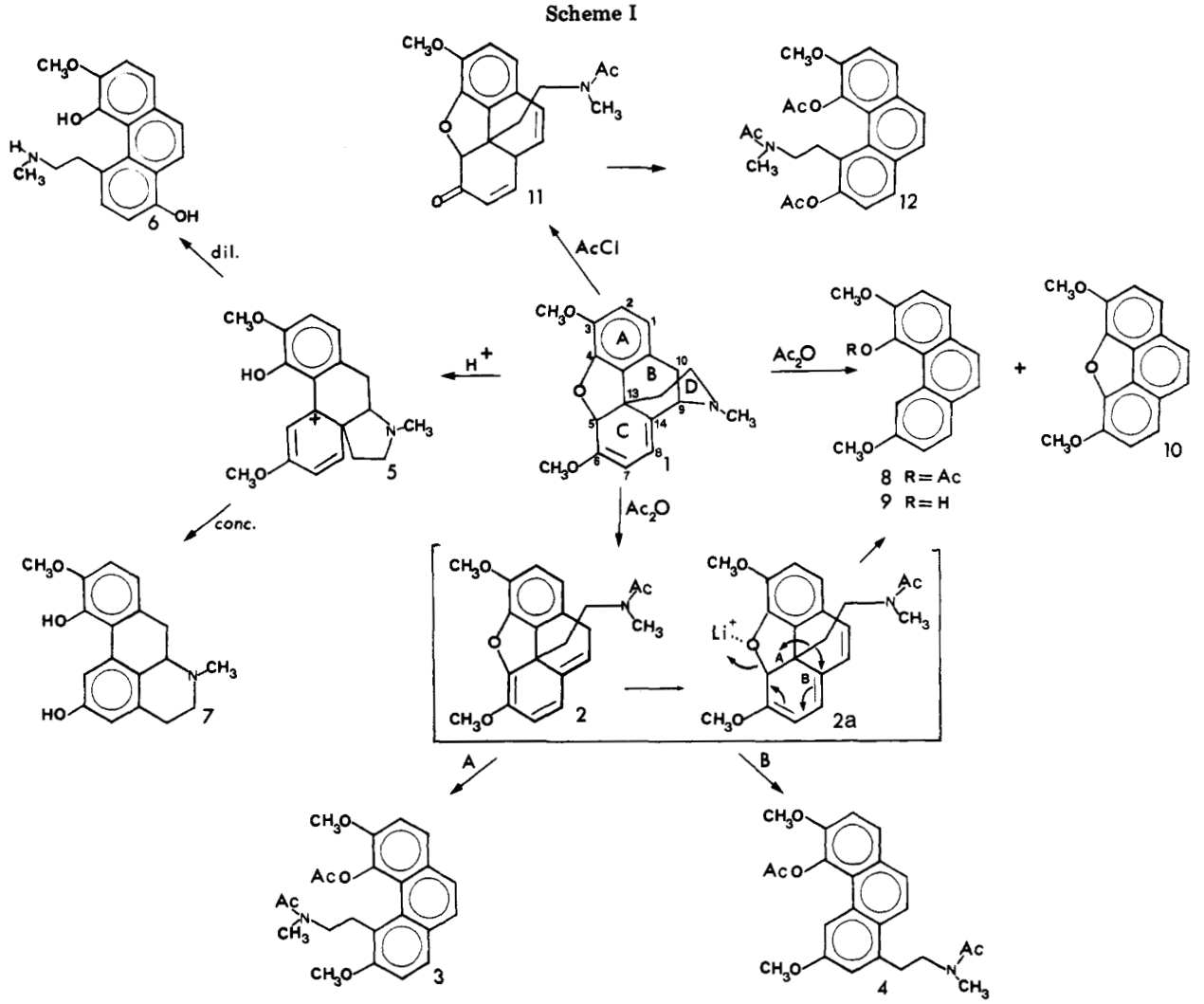
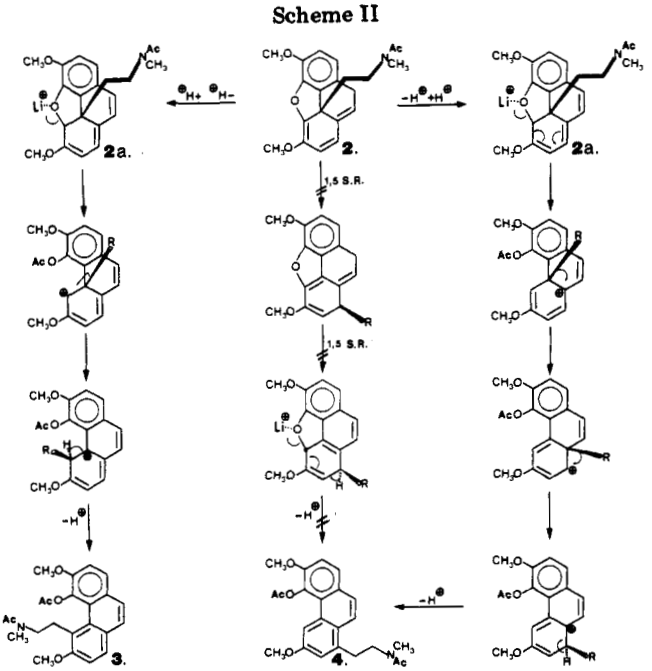
(8) (a) Bentley, K. W. In "The Alkaloids"; Manske, R. H. F., Ed.; Academic Press: New York, 1971; Vol. XIII, p 16.
(9) Santavy, F. In "The Alkaloids"; Manske, R. H. F., Rodrigo, R., Eds.; Academic Press: New York, 1979; Vol. XVII, p 426.
(10) Stork, G. In "The Alkaloids"; Manske, R. H. F., Holmes, H. L., Eds.; Academic Press: New York, 1952; Vol. II, p 193.

Scheme I



Scheme II



stabilized carbocation at C-5. Migration of the 2-(*N*-methylacetamido)ethyl side chain from C-13 to C-5, concomitant with a proton loss at C-5, results in the fully aromatized **3**. We propose two possible pathways for the formation of **4** from **2**. Although **4** may be thought of as the result of two 1,5-sigmatropic rearrangements followed by epoxide opening and a proton loss from **2** (Scheme II), the neutral intermediates could not be detected by GC–MS. A more plausible mechanism for the formation of **4** (Scheme II) involves opening of the epoxide in **2a** followed by a 2-carbon migration of the 2-(*N*-methylacetamido)ethyl side chain from C-13 to C-8. The attractiveness of this pathway is supported by the subsequent formation of two resonance stabilized carbocations at C-14 and C-8, concomitant with a proton loss at C-8, resulting in a fully aromaticized **4**.

Opening of the epoxide in **2a** may lead to other transformations, such as loss of the 2-(*N*-methylacetamido)ethyl side chain at C-13 to yield **8** and **9**, both detectable in illicit heroin. It has also been noted that **8** and **9** may arise directly from **1** by a concerted elimination of the 2-(*N*-methylacetamido)ethyl side chain and cleavage of the C-5 to O bond in a "push–pull" mechanism.[11]

Spectroscopic Characterization of 3 and 4. The IR spectrum of **3** and **4** exhibited intense bands at 1645 and 1640 cm^{-1}, respectively, due to ν C=O of the amide moiety. Intense bands at 1760 cm^{-1} in **3** and 1705 cm^{-1} in **4** were assigned to the ν C=O of the aromatic ester carbonyls.

High-resolution electron-impact mass spectral analysis established that the compositions of **3** and **4** were identical ($C_{23}H_{25}NO_5$). Furthermore, exact mass measurement of the m/z 100 fragment ion in **3** identifed it as $C_5H_{10}NO$,

(11) Sork, G. In "The Alkaloids"; Manske, R. H. F., Holmes, H. L., Eds.; Academic Press: New York, 1952; Vol. II, p 193.

resulting from the 2-(*N*-methylacetamido)ethyl side chain. Absence of this ion in **4** was inferred to result from a lack of steric crowding, a condition that exists in the "bay" location of **3**. A prominent ion in **3** at m/z 87 can be accounted for when the side chain is flanked by an acetoxy group.[12] The mass spectral characterization of **3** and **4** was also confirmed by the study of analogous phenanthrene compounds.[13]

The ^{1}H NMR analysis of the aromatic hydrogens on **4** showed a remote downfield shift resonance for one "bay" proton (H-5). Conversely, **3** did not exhibit this shift, implicating the presence of non-hydrogen substituents at C-4 and C-5. An in-depth characterization of **3** and **4** by ^{1}H NMR was difficult due to time dependent states associated with the hindered rotation of the amide moiety.[14] Therefore, both **3** and **4** were subjected to reduction with lithium aluminum hydride to yield 3,6-dimethoxy-4-hydroxy-5-[2-(*N*-methyl-*N*-ethylamino)ethyl]-phenanthrene (**13**), and 3,6-dimethoxy-4-hydroxy-8[2-(*N*-methyl-*N*-ethylamino)ethyl]phenanthrene (**14**), respectively. The ^{1}H NMR spectra of **3** and **4** were first order. Decoupling difference spectra experiments applied to the methyl ethers (long range coupled to C-2 and C-7) were effective in establishing their C-3 and C-6 locations. Nuclear Overhouser enhancement difference spectra (NOEDS) analyses of both **3** and **4** and their reduced counterparts confirmed that the 2-(*N*-methylacetamido)-ethyl side chain was located at C-5 in **3** and at C-8 in **4**.

Identification of 2. Although an analogous compound of **2** has been previously reported[4] (compound **11**) and does provide a precedence for the structural assignment of **2** it does not provide direct proof. Therefore it was desirable to confirm the presence of compound **2** as a byproduct resulting from the action of acetic anhydride upon **1**. The structure of **2** was established by ^{1}H NMR. It was conceptually attractive to envision opening of the D ring as in a Hoffmann degradation of morphine or codeine. This would place the resulting double bond C-9 to C-10 and extend conjugation from ring A through ring C in the thebaine complement. Our studies,[15] and others,[16] involving the reaction of acetic anhydride with morphine and codeine have confirmed opening of the D ring with concomitant introduction of a double bond at C-9 to C-10. However, the ^{1}H NMR of **2** showed a decided absence of an H-5 resonance while maintaining the aliphatic resonances of H-10$_\alpha$ and H-10$_\beta$. These findings preclude the existence of a C-9 to C-10 double bond and are consistent with structure **2**. The EI mass spectral analysis of **2** confirmed the ^{1}H NMR findings by yielding a molecular ion at m/z 353 (see Experimental Section for detailed ^{1}H NMR and mass spectral data).

Experimental Section

General Procedures. Evaporations were done in a Buchi rotary evaporator in vacuo at a temperature of 70 °C. Melting points were determined on a Thomas-Hoover apparatus (capillary method) and were uncorrected. All high-performance liquid chromatography (HPLC) was done on a Waters Model 6000A, utilizing a Sorbax ODA analytical column measuring 16 cm × 4.6 mm id and interfaced with a 254-nm UV detector. Preparative HPLC was done on a Sorbax column measuring 25 cm × 21.2 mm id and interfaced with a refractive index detector. The solvent system used was acetonitrile:water (40:60) at a flow rate of about 10 mL/min. Gas chromatography was performed on a Finnigan 9600 instrument equipped with a Grob capillary injection system. The fused silica capillary column (Hewlett-Packard) measured 12 M × 0.20 mm id and was coated with cross-linked OV-1. Helium was used as the carrier gas at a head pressure of 12 psi. All samples were injected with a 40/1 split ratio and an injection port temperature of 230 °C. Infrared (IR) spectra were recorded in KBr using a Beckman 4240 spectrophotometer. Nuclear magnetic resonance (^{1}H NMR) spectra were obtained on a Nicolet-NT-200WB-FT spectrometer (200 MHz) equipped with an NIC-1180 data system and a Model 293A pulse programmer. All spectra were recorded in $CDCl_3$ with Me_4Si as internal standard. ^{1}H NMR experiments were performed as outlined by Hall and Sanders.[17] The low-resolution mass spectrometer used was a Finnigan 4600 quadrupole mass analyzer operating under EI conditions at 70 eV. Accurate mass measurements were also obtained under EI conditions with a Kratos MS-30 double focusing mass analyzer of Neir-Johnson geometry and utilizing the dual beam mode with direct sample introduction. The elemental analysis was performed by Galbraith Laboratories, Knoxville, TN.

$\Delta^{5,7,9(14)}$-*N*-Acetyldesthebaine (2). A mixture of **1** (2.0 g), anhydrous magnesium sulfate (1.20 g), and acetic anhydride (30.0 mL) was stirred and heated at 90–100 °C for 2 h. Evaporation of the Ac_2O left a light orange residue. The residue was dissolved in 100 mL of Et_2O:CH_2Cl_2 (60:40) and washed successively with 1 M Na_2CO_3, 0.5 N H_2SO_4, and 1 M Na_2CO_3. The organic layer was dried (Na_2SO_4) and evaporated to yield **2** as an oil (1.14 g, 57%). Isolation of **2** from other byproducts of **1** was accomplished by HPLC: ^{1}H NMR C_1-H and C_2-H (m, 2, δ 6.886–6.727), C_7-H and C_8-H (m, 2, δ 6.151–6.082), C_7-H (d, 1, J_{7-8} = 9.5 Hz, δ 5.864–5.776), CH_3O^6 (d, 3, J = 1.25 Hz, δ 4.000), CH_3O^3 (d, 3, J = 1.38 Hz, δ 3.953), C_{16}-H_2 (m, 2, δ 3.465–3.187), CH_3N (d, 3, δ 2.837–2.777), CH_3CN (d, 3, δ 1.924), and C_{15}-H_2 (m, 2, δ 1.903–1.488); mass spectrum, m/z (relative intensity) $M^{+\cdot}$ 353 (100), 280 (20), 265 (27), 252 (20), 237 (19), 152 (8), 101 (50), 86 (57), 44 (96), and 43 (23). Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96; O, 18.11. Found: C, 70.0; H, 6.86; N, 3.78; O, 19.5.

3,6-Dimethoxy-4-acetoxy-5-[2-(*N*-methylacetamido)-ethyl]phenanthrene (3). Compound **1** (3.0 g) was dissolved in Ac_2O (50 mL) containing LiCl (2 g). The solution was stirred for 6 h at 100 °C. The solvent was evaporated in vacuo (10 mmHg) at 70 °C. The residue was dissolved in Et_2O:CH_2Cl_2 (60:40) (100 mL) and washed successively with 1 M Na_2CO_3, 0.5 N H_2SO_4, and 1 M Na_2CO_3. The organic layer was dried (Na_2SO_4) and evaporated to an oil. HPLC analysis showed a 70:20:10 mixture of **8**, **3**, and **4**, respectively. The oil was dissolved in *i*-prOH and crystallization allowed to proceed overnight, resulting in the removal of about one-half of **8** and **4**. Alternatively, the oil was dissolved in Et_2O and chromatographed on neutral alumina, using Et_2O to elute **8** and Et_2O:CH_2Cl_2 (60:40) to elute **3** and **4**. Separation of **3** and **4** was accomplished by preparative HPLC. The isolated **3** was passed through neutral alumina to remove color. Solvent removal yielded **3** as a white crystalline product (370 mg, 10–15%): mp 141.0–141.5 °C; ^{1}H NMR (temperature dependent states—amide) C_1-H (d, 1, J = 8.8 Hz, δ 7.715 and 7.686), C_8-H (d, 1, J_{8-7} = 8.7 Hz, δ 7.633 and 7.605), C_9-H (d, 1, J_{9-10} = 8.7 Hz, δ 7.374), C_{10}-H (d, 1, J_{10-9} =*8.7 Hz, δ 7.321), C_2-H (d, 1, J_{2-1} = 8.8 Hz, δ 7.321 and 7.302), C_7-H (d, 1, J_{7-8} = 8.7 Hz, δ 7.232 and 7.221), CH_3O^6 (s, 3, δ 4.017 and 3.986), CH_3O^6 (s, 3, δ 3.944), CH_2 (m, 2, δ 3.525), CH_2 (br, m, 2, δ 3.552–2.776), NCH_3 (s, 3, δ 2.532 and 2.103), CH_3CO (s, 3, δ 2.11), and CH_3CN (s, 3, 1.602 and 1.444); IR (cm^{-1}) 1760, 1645, 1210, 1200, 1025, and 840; high-resolution mass spectrum, empirical composition, m/z (relative intensity) calcd for $C_{23}H_{25}NO_5$ m/z 395.1733 ($M^{+\cdot}$), found m/z 395.1735 (21), calcd for $C_{21}H_{23}NO_4$ m/z 353.1627, found m/z 353.1647 (48), calcd

(12) See ref 2.

(13) The mass spectral and ^{1}H NMR characterization of **3** and **4** was aided by the study of similar phenanthrene compounds: (a) 3-methoxy-4,6-diacetoxy-8-[2-(*N*-methylacetamido)ethyl]phenanthrene, (b) 3-methoxy-4,8-diacetoxy-5-[2-(*N*-methylacetamido)ethyl]phenanthrene, (c) 3,4-diacetoxy-8-[2-(*N*-methylacetamido)ethyl]phenanthrene, (d) 3-methoxy-4,6-diacetoxy-5-[2-(*N*-methylacetamido)ethyl]phenanthrene, (e) 3-methoxy-4-acetoxy-8-[2-(*N*-methylacetamido)ethyl]phenanthrene.

(14) Frankel, G.; Cava, M. P.; Dalton, D. R. *J. Am. Chem. Soc.* **1976**, *89*, 329 and references cited therein.

(15) Compounds characterized as a result of the action of acetic anhydride on morphine or codeine: (a) α-methylmorphimethine, (b) O^3,O^6-diacetyl-α-methylmorphimethine, (c) α-methylcodimethine, (d) O^6-acetyl-α-methylcodimethine, and (e) *N*-acetylcodimethine.

(16) Klein, M., unpublished results.

(17) Hall, L. D.; Sanders, K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703.

for $C_{18}H_{16}O_3$ m/z 280.1099, found m/z 280.1096 (69), calcd for $C_{17}H_{13}O_3$ m/z 265.0865, found m/z 265.0878 (100), calcd for $C_{16}H_{12}O_3$ m/z 252.0786, found m/z 252.0801 (74), calcd for $C_5H_{10}NO$ m/z 100.0762, found m/z 100.0771 (12), calcd for C_4H_9NO m/z 87.0684, found m/z 87.0678 (12), calcd for C_4H_8NO m/z 86.0606, found m/z 86.0617 (12), calcd for C_2H_6N m/z 44.0500, found m/z 44.0520 (99), and calcd for C_2H_3O m/z 43.0184, found m/z 43.0202 (55). Anal. Calcd for $C_{23}H_{25}NO_5$: C, 69.85; H, 6.37; N, 3.54; O, 20.22. Found: C, 69.84; H, 6.42; N, 3.51; O, 20.39.

3,6-Dimethoxy-4-acetoxy-8-[2-(*N*-methylacetamido)ethyl]phenanthrene (4). The preparation and isolation of **4** can be accomplished as described for **3**. However, it was more conveniently prepared by the rearrangement of **1** with methanesulfonic acid[18] followed by treatment with Ac_2O:[19] mp 137–138 °C; ^1H NMR (temperature dependent states—amide) C_5-H (d, 1, J_{5-7} = 2.5 Hz, δ 8.630 and 8.609), C_9-H (d, 1, J_{9-10} = 9.1 Hz, δ 7.943 and 7.692), C_1-H (d, 1, J_{1-2} = 8.8 Hz, δ 7.774 and 7.764), C_{10}-H (d, 1, J_{10-9} = 9.2 Hz, δ 7.588), C_2-H (d, 1, J_{2-1} = 8.8 Hz, δ 7.380 and 7.361), C_7-H (d, 1, J_{7-5} = 2.5 Hz, δ 7.134 and 7.051), CH_3O^6 (s, 3, δ 3.978 and 3.971), CH_3O^3 (s, 3, δ 3.961), CH_2 (m, 2, δ 3.702–3.587), CH_2 (m, 2, δ 3.345–3.270), NCH_3 (3, s, δ 2.997 and 2.795), CH_3CO (s, 3, δ 2.529) and CH_3CN (s, 3, δ 2.083 and 1.853); IR (cm^{-1}) 1705, 1640, 1600, 1060, 1270, 1200, and 825; high-resolution mass spectrum, empirical composition, m/z (relative intensity) calcd for $C_{23}H_{25}NO_5$ m/z 395.1733 ($M^{+\cdot}$), found m/z 395.1757 (16), calcd for $C_{21}H_{23}NO_4$ m/z 353.1627, found m/z 353.1623 (16), calcd for $C_{18}H_{16}O_3$ m/z 280.1099, found m/z 280.1093 (79), calcd for $C_{17}H_{13}O_3$ m/z 265.0865, found m/z 265.0844 (11), calcd for $C_{16}H_{12}O_3$ m/z 252.0786, found m/z 252.0817 (3), calcd for C_4H_8NO m/z 86.0606, found m/z 86.0618 (11), calcd for C_2H_6N m/z 44.0500, found m/z 44.0528 (100), and calcd for C_2H_3O m/z 43.0184, found m/z 43.0215 (19). Anal Calcd for $C_{23}H_{25}NO_5$: C, 69.85; H, 6.37; N, 3.54; O, 20.22. Found: C, 69.68; H, 6.52; N, 3.52; O, 20.28.

3,6-Dimethoxy-4-hydroxy-5-[2-(*N*-methyl-*N*-ethylamino)ethyl]phenanthrene (13). Compound **3** (150 mg) was dissolved in $CHCl_3$ (2 mL) followed by the addition of Et_2O (15 mL) and an excess of $LiAlH_4$ (50 mg). The solution was heated at 30 °C for 30 min, cooled, and extracted with 0.5 N H_2SO_4 to isolate the reduced tertiary amine. The acid was extracted with $CHCl_3$ to remove unreacted **3** and then basified with $NaHCO_3$ and reextracted with $CHCl_3$ for the isolation of **13**. The $CHCl_3$ extract was dried (Na_2SO_4) and then evaporated to give a residue which was recrystallized from Et_2O to give 100 mg **13** (75%): mp 159–161 °C; ^1H NMR C_8-H (d, 1, J_{8-7} = 8.5 Hz, δ 7.57), C_9-H (s, 1, δ 7.28), C_{10}-H (s, 1, δ 7.26), C_1-H (d, 1, J_{1-2} = 8.5 Hz, δ 7.23), C_7-H (d, 1, J_{7-8} = 8.6 Hz, δ 7.18), C_2-H (d, 1 J_{2-1} = 8.5 Hz, δ 7.02), CH_3O^3 (s, 3, δ 3.97), CH_3O^6 (s, 3, δ 3.60), CH_2C_5 (t, 2, J = 7.5, δ 3.43), CH_2N (q, 2, J = 7.5 Hz, δ 2.49), CH_3CH_2N (t, 2, J = 7.2, δ 2.44), CH_3CH_2N (t, 3, J = 7.2 Hz, δ 1.01), and CH_3N (s, 3, δ 2.26); IR (cm^{-1}) 1500, 1420, 1282, 1272, 1243, 1145, 1021, 825, and 760; mass spectrum, M/z (relative intensity) $M^{+\cdot}$ 339 (17), 280 (8), 265 (5), 252 (2), 72 (100), and 44 (13). Anal Calcd for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13; O, 14.14. Found: C, 74.19; H, 7.37; N, 4.02; O, 14.56.

3,4-Dimethoxy-4-hydroxy-8-[2-(*N*-methyl-*N*-ethylamino)ethyl]phenanthrene (14). Compound **14** was prepared from **4** and isolated as described for **13** (100 mg, 75%): mp 123–125 °C; ^1H NMR C_5-H (d, 1, J_{5-7} = 2.5 Hz, δ 9.207), C_9-H (d, 1, J_{9-10} = 9.2 Hz, δ 7.766), C_{10}-H (d, 1, J_{10-9} = 9.3 Hz, δ 7.518), C_1-H (d, 1, J_{1-2} = 8.60 Hz, δ 7.409), C_2-H (d, 1, J_{2-1} = 8.5 Hz, δ 7.279), C_7-H (d, 1, J_{7-5} = 2.6 Hz, δ 7.116), CH_3O^3 (s, 3, δ 4.054), CH_3O^6 (s, 3, δ 3.989), CH_2C_8 (m, 2, δ 3.28), CH_2N (m, 2, δ 2.766), CH_3CH_2N (q, 2, J = 7.17, δ 2.609), CH_3CH_2N (t, 3, J = 7.14 Hz, δ 1.142), and CH_3N (s, 3, δ 2.434); IR (cm^{-1}) 1595, 1425, 1275, 1205, 1145, 1118, 1060, and 810; mass spectrum, m/z (relative intensity) $M^{+\cdot}$ 339 (12), 267 (2), 252 (1), 72 (100), and 44 (12). Anal Calcd for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13; O, 14.14. Found: C, 74.16; H, 7.52; N, 4.04; O, 14.12.

3,6-Dimethoxy-4,5-epoxyphenanthrene (10). Compound **2** (0.5 g), MeOH (20 mL), and $NaOCH_3$ (0.1 g) were stirred and warmed at 40 °C for 1 h. The solvent was evaporated leaving a light orange oil. The residue was dissolved in Et_2O and extracted with 0.5 N H_2SO_4 and 0.5 N $NaHCO_3$. The Et_2O extract, after drying ($MgSO_4$), was passed through neutral alumina. Evaporation of the solvent left **10** as a white crystalline product: 350 mg (70%); mp 106–123 °C; ^1H NMR C_9-H and C_{10}-H (s, 2, δ 7.726), C_1-H and C_8-H (d, 2, J = 8.2 Hz, δ 7.676), C_2-H and C_7-H (d, 2, J = 8.2, δ 7.380), and $CH_3O^{3,6}$ (s, 6, δ 4.359); IR (cm^{-1}) 1632, 1492, 1260, 1245, 1030, 815, and 581; mass spectrum, m/z (relative intensity) $M^{+\cdot}$ 252 (86), 237 (100), 194 (21), and 138 (15).

Rearrangement of $\Delta^{5,7,9(14)}$-*N*-Acetyldesthebaine (2). Compound **2** was isolated via HPLC according to the conditions outlined above. To lithium chloride (50 mg) in acetic anhydride (2 mL) was added 100 mg of compound **2**. The solution was heated for 1 h at 100 °C. After removal of the excess acetic anhydride, **3** (20%), **4** (9%), and **8** (70%) were isolated by HPLC. The MS, IR, and ^1H NMR spectra obtained for **3**, **4**, and **8**, were identical to the MS, IR, and ^1H NMR spectra obtained from products which were isolated from the direct acetylation reaction of thebaine.

Registry No. **1**, 115-37-7; **2**, 91295-73-7; **3**, 89469-84-1; **4**, 91295-74-8; **8**, 47192-97-2; **10**, 4504-42-1; **13**, 91295-75-9; **14**, 91295-76-0.

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