Sequential Dehydrogenation of 3-Keto-4-azasteroids. The Reaction of Ene-Lactams with 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)

J. Michael Williams,* George Marchesini, Robert A. Reamer, Ulf-H. Dolling, and Edward J. J. Grabowski

Department of Process Research, Merck Research Laboratories, Division of Merck & Co., Inc., Rahway, New Jersey 07065

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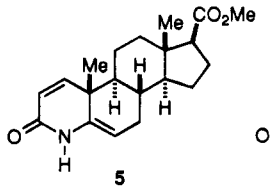
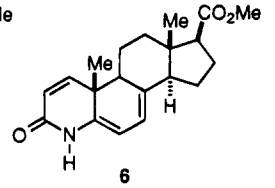
The identification of Δ^1-3-keto-4-azasteroids as potent inhibitors of the enzyme 5α-reductase[1] led to the the first drug therapy, Proscar, for the treatment of benign prostatic hyperplasia (BPH).[2] A process for the large-scale production of finasteride, the active agent in Proscar, required a practical method for the dehydrogenation of 3-keto-4-azasteroids introducing unsaturation at C1. A novel method using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was developed for this purpose, and this process is now used to manufacture finasteride on multi-kilogram scale.[3] It was the identification of overoxidation products in this process that prompted us to develop a controlled method for the dehydrogenation of Δ^1-3-keto-4-azasteroids using electrochemical oxidation followed by reaction of the resulting $\Delta^{1,5}$-3-keto-4-azasteroid with DDQ. It is the details of this study that we now wish to disclose.

The reaction of the 3-keto-4-azasteroid **1** with DDQ in the presence of bis(trimethylsilyl)trifluoroacetamide (BSTFA) and catalytic triflic acid in toluene at 25 °C gives the diastereomeric C–C adducts **2** which have been well characterized.[3] After thermolysis, a 93% yield of product **3** and 2–3 % of the C–O adduct **4** are observed. An excess of DDQ (1.25 equiv) is used in order to expedite the bimolecular adduct formation. Residual DDQ is quenched with methyl acetoacetate prior to thermolysis at 110 °C, minimizing the formation of overoxidation products. Using this protocol, less than 1% each of three overoxidation products, **5**–**7**, are formed.



5



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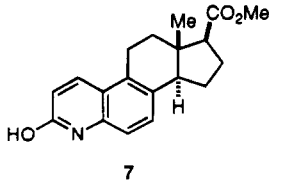

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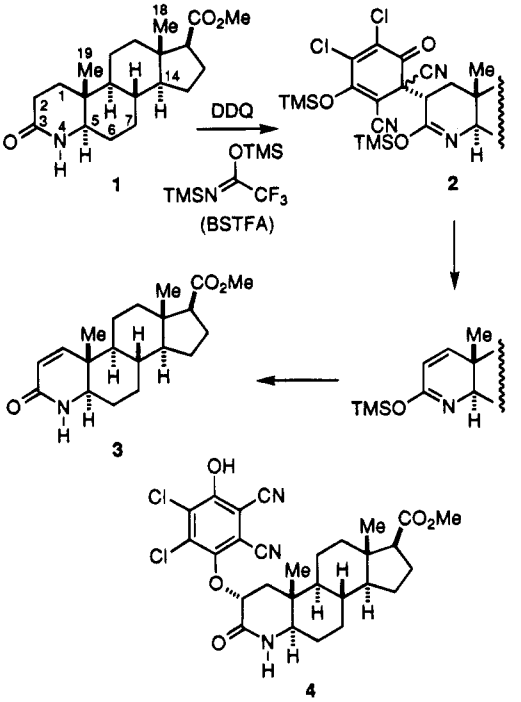
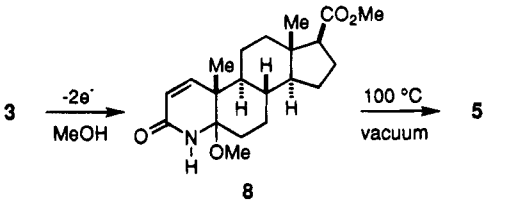
Scheme 1



An interest in preparing reference samples of these compounds led us to consider how they might be made selectively. We were unable to introduce the Δ^5 double bond in a controlled fashion using DDQ; attempts to convert **1** or **3** to **5** were unsuccessful. Under forcing conditions a complex mixture of products was observed.

To prepare **5** we turned to the well-precedented anodic oxidation of lactams to obtain **8** with the elimination of methanol to generate the Δ^5 double bond.[4] Electrochemical oxidation cleanly afforded the desired product which was isolated by crystallization from methanol/water. Heating to 100 °C under vacuum resulted in the expulsion of methanol to give the desired product.[5] To our knowledge these reactions have not been applied to an unsaturated lactam.



An initial attempt to make $\Delta^{1,5,7}$-3-keto-4-azasteroid **6** by subjecting **5** to reaction with BSTFA and catalytic triflic acid in toluene followed by DDQ gave none of the desired product. ^{1}H and ^{13}C NMR revealed that the reaction of **5** with BSTFA gives a 60:40 mixture of *O*-silyl imidate **9** and *N*-silyl lactam **10**.[6] Reaction with DDQ affords a mixture of diastereomeric C6–O adducts **11a** and **11b** (85:15).[7] The structures were assigned based on long-range ^{1}H–^{13}C correlation data, obtained in a

(1) (a) Rasmusson, G. H.; Reynolds, G. F.; Utne, T.; Jobson, R. B.; Primka, R. L.; Berman, C.; Brooks, J. R. *J. Med. Chem.* **1984**, *27*, 1690–1701. (b) Rasmusson, G. H.; Reynolds, G. F.; Steinberg, N. G.; Walton, E.; Patel, G. F.; Liang, T.; Cascieri, M. A.; Cheung, A. H.; Brooks, J. R.; Berman, C. *J. Med. Chem.* **1986**, *29*, 2298–2315.

(2) Gormley, G. J. et al. *N. Engl. J. Med.* **1992**, *327*, 1185–1191.

(3) Bhattacharya, A.; DiMichele, L. M.; Dolling, U.-H.; Douglas, A. W.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1988**, *110*, 3318–3319.

(4) Shono, T.; Matsumura, Y.; Uchida, K.; Kobayashi, H. *J. Org. Chem.* **1985**, *50*, 3243–3245 and references cited therein.

(5) (a) Bohme, H.; Berg, G. *Chem. Ber.* **1966**, *99*, 2127–2135. (b) Nyberg, K. *Synthesis* **1976**, 545–546. (c) Shono, T.; Matsumura, Y.; Tsubata, K.; Sugihara, Y.; Yamane, S.-i.; Kanazawa, T.; Aoki, T. *J. Am. Chem. Soc.* **1982**, *104*, 6697–6703.

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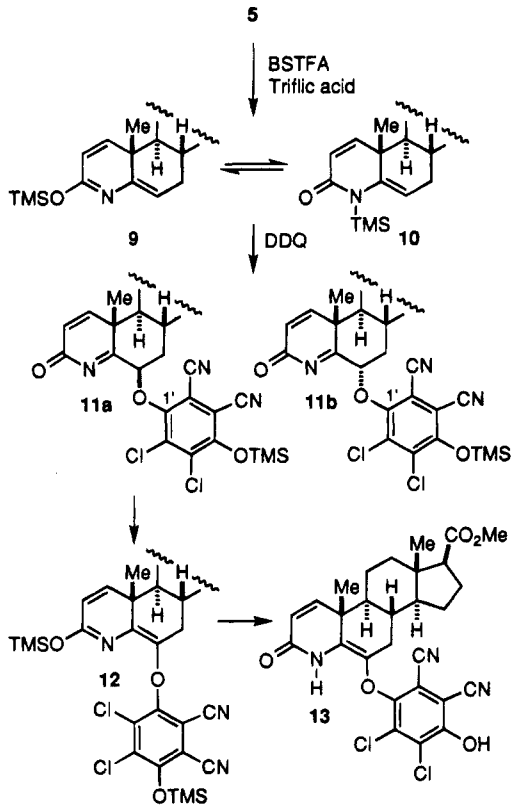
Scheme 2



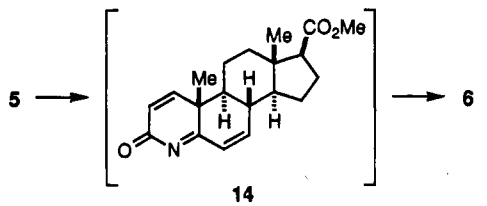
HMBC experiment[8], which established the proximity of C6-H and C1′ (three-bond coupling constant J = 3.2 Hz obtained in a ^{1}H-coupled ^{13}C spectrum) and the C19 methyl and C5 (three-bond pathway). The stereochemical assignment of the DDQ moiety is based on C6-H to C7-H_2 coupling constants. In **11a**, C6-H is a triplet (J = 3.2 Hz) consistent with an equatorial orientation of the proton. In **11b**, C6-H is a doublet of doublets (J = 12.9, 6.7 Hz) indicative of an axial proton. Silylation under the reaction conditions afforded **12** (^{29}Si NMR (49.7 MHz) δ 30.45, 21.82). Solvolysis gave **13** which was isolated in 49% yield and fully characterized. Less than 10% dehydrogenation is observed under these conditions.

Considering the first observation of **6** in the dehydrogenation of **1**, the failure to convert **5** to **6** under similar conditions was surprising. In the reaction of silyl enol ethers it had been shown that carbon adduct formation leading to dehydrogenation is favored by polar solvents and lower temperatures.[9] Silylation of **5** in acetonitrile produced a 40:60 mixture of silyl imidate **9** and silyl lactam **10** that was reacted with DDQ. The predominant process observed was dehydrogenation with the C6–O adducts **11a** and **11b** (46:54), accounting for less than 30% of the product mixture.

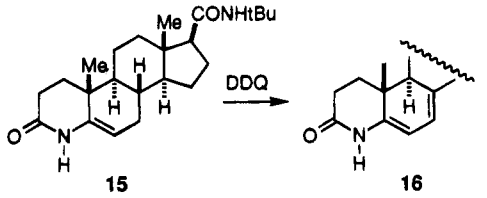
Subsequently it was found that silylation is not required to achieve dehydrogenation. The $\Delta^{1,5}$-azasteroid **5** was slurried in acetonitrile, and DDQ was added at −40 °C producing a deep purple color.[10] The reaction was allowed to warm to room temperature at which point the mixture became a yellow-orange solution from which the bright yellow product **6** crystallized.

The reaction conversion in acetonitrile proved to be variable most likely as a result of the reaction mixture being nonhomogeneous. Both the conversion and the purity of the isolated product were improved by adding a solution of DDQ in acetonitrile to a solution of steroid in dichloromethane. The mixture remains homogeneous until it is warmed to −25 °C at which point the hydroquinone product (H_2-DDQ) begins crystallizing. After warming to 22 °C and filtering to remove the hydroquinone, the product is crystallized by replacing the dichloromethane with acetonitrile on a rotary evaporator. Using this protocol, **6** was obtained analytically pure in 66% yield.

An NMR study provided some information concerning the course of this reaction. On adding a solution of DDQ (1.0 equiv) in acetonitrile-d_3 to a solution of **5** in dichloromethane-d_2 at −40 °C, 90% of the ene-lactam was consumed within 5 min. The predominant product was identified as the $\Delta^{1,4,6}$-3-keto-4-azasteroid **14**.[11] Addition of triethylamine prior to warming prevented acid-catalyzed tautomerization.



To assess the potential for more general application we subjected an ene-lactam lacking the Δ^1 double bond to the reaction conditions developed for the dehydrogenation of **5**. Δ^5-3-Keto-4-azasteroids are readily available and potentially serve as intermediates in the preparation of more highly functionalized azasteroids.[12] The treatment of **15** with DDQ afforded a 58% isolated yield of **16**.



Reiteration of the reaction allows controlled sequential dehydrogenation. The treatment of **6** with DDQ in acetonitrile/dichloromethane provided **17** in 49% yield. The position of the double bond in **17** was determined with the data from a HMBC experiment where a correlation was observed from the C18 methyl protons to

(6) Selected NMR data in toluene-d_8. **9**: ^{1}H NMR (400.1 MHz) δ 6.02 (d, J = 9.5, 1H), 5.77 (d, J = 9.5, 1H), 5.59 (dd, J = 5.6, 2.8, 1H), 0.43 (s, 9H); ^{13}C NMR (100.6 MHz) δ 156.6 (C3); ^{29}Si NMR (49.7 MHz) δ 20.75. **10**: 1H NMR (400.1 MHz) δ 6.02 (d, J = 9.5, 1H), 5.70 (d, J = 9.5, 1H), 4.77 (dd, J = 5.2, 2.0, 1H), 0.33 (s, 9H); ^{13}C NMR (100.6 MHz) δ 169.1 (C3); ^{29}Si NMR (49.7 MHz) δ 11.95.

(7) Similarly, the reaction of a $\Delta^{1,3,5}$-3-benzoyloxy steroid with DDQ resulted in axial O-adduct formation at C6 with transfer of benzoyl to the hydroquinone moiety: Reimann, H.; Jaret, R. S. *Can. J. Chem.* **1970**, *48*, 1478–1479.

(8) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093–2094.

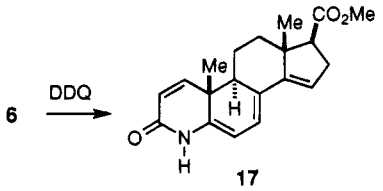
(9) Bhattacharya, A.; DiMichele, L. M.; Dolling, U.-H.; Grabowski, E. J. J.; Grenda, V. J. *J. Org. Chem.* **1989**, *54*, 6118–6120.

(10) The color observed suggests formation of a charge transfer complex as observed in the reaction of DDQ with other electron donor species such as silyl enol ethers. See reference 9.

(11) NMR data for **14**: ^{1}H NMR (CD_3CN, 400.1 MHz) δ 7.13 (d, J = 9.9, 1H), 6.69 (d, J = 9.9, 2.0, 1H), 6.198 (dd, J = 9.9, 3.0, 1H), 6.197 (d, J = 9.9, 1H), 1.18 (s, 3H), 0.70 (s, 3H); ^{13}C (CD_3CN, 100.6 MHz) δ 190.4, 174.4 172.1, 152.2, 150.5, 129.4, 123.4, 54.9, 52.8, 51.8, 48.9, 44.8, 41.8, 38.8, 37.9, 24.1, 23.8, 21.4, 20.4, 13.4.

(12) Δ^5-3-Keto-4-azasteroids are prepared from the keto acid by reaction with a source of ammonia at high temperature. See reference 1b and references cited therein.

C14, a fully substituted sp^2 carbon. If, however, **6** was first treated with BSTFA and catalytic triflic acid in toluene, the addition of DDQ at 20 °C resulted in both dehydrogenation to give **17** as the major product and loss of the C19 methyl leading to **7** (50 and 24% yields after chromatography, respectively). This observation suggests a possible source of **7** in the dehydrogenation of **1**. DDQ is not required for the formation of **7**; treatment of **6** with BSTFA/triflic acid in toluene followed by exposure to air at 100 °C provided a 31% yield of the aromatic product after solvolysis.



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Discussion

There is an inherent problem in the dehydrogenation of a lactam to make an ene-lactam in that the product is more easily oxidized than is the lactam. The problem has been addressed using anodic oxidation in which methanol intercedes to prevent further oxidation. This approach, however, cannot be applied in an iterative fashion. Attempts to extend this method to the preparation of **6** were unsuccessful giving a complex mixture of products.[13] In analysis of the problem, other oxidants were considered that would produce discrete intermediates which could be subsequently converted to the homologous ene-lactam under nonoxidizing conditions. Bromination in methanol followed by dehydrobromination and elimination of methanol appeared to have some potential for success, but formation of the $\Delta^{1,5}$-3-keto-6-bromo-4-azasteroid was of some concern based on a recent account.[14] Even if successful, the implementation of such a scheme would be cumbersome. No method for the direct dehydrogenation of an ene-lactam is available.

The use of DDQ offers a direct method for accomplishing this transformation which is controlled. Although the formation of C−C adducts as observed in the reaction of silyl enol ethers with DDQ could account for the observed control, we have been unable to characterize C−C adducts leading to dehydrogenation. If such adducts are formed, *thermolysis* is a very facile process taking place below −25 °C. We believe that the method reported herein is successful because DDQ reacts rapidly with the ene-lactam to give the Δ^4-3-keto-4-azasteroid which does not react readily with DDQ under conditions where subsequent tautomerization to the Δ^5-3-keto-4-azasteroid is slow.

The factors influencing the course of these reactions to give dehydrogenation or unproductive C−O adduct formation are not understood at this point. It is clear that the choice of solvent has a marked influence on the reaction. Silylation of the ene-lactam does not change the course of the reaction in a more polar solvent. In toluene, silylation is required to solubilize the azasteroid; an attempt to conduct the reaction of **5** with DDQ in toluene without silylation was not successful.

(13) Anodic oxidation of enol esters, isoelectronic with ene-lactams, are not generally synthetically useful. Shono, T.; Matsumura, Y.; Nakagawa, Y. *J. Am. Chem. Soc.* **1974**, *96*, 3532−3536.

(14) (a) Shono, T.; Terauchi, J.; Ohki, Y.; Matsumura, Y. *Tetrahedron Lett.* **1990**, *31*, 6385−6386. However, chlorination of a $\Delta^{1,5}$-3-keto-6-chloro-4-azasteroid gave the $\Delta^{1,5}$-3-keto-6-chloro-4-azasteroid. (b) Back, T. G.; Chau, J. H.-L.; Dyck, B. P.; Gladstone, P. L. *Can. J. Chem.* **1991**, *69*, 1482−1486.

Conclusions

A practical method for the controlled, sequential dehydrogenation of 3-keto-4-azasteroids using electrochemical oxidation followed by reaction with DDQ has been demonstrated making highly unsaturated azasteroids available.

Experimental Section

General Procedures. Solvents were dried over 4 Å molecular sieves to a water content of less than 0.1 mg/mL as determined by Karl Fischer titration. The Δ^5-3-keto-4-azasteroids are relatively stable as crystalline solids but are particularly sensitive to oxygen in solution. For example, after exposure of a solution of **6** in dichloromethane to air for 20 min, the bright yellow color characteristic of **6** was almost completely gone. Care should be taken to purge solvents of oxygen and maintain reaction mixtures under an inert atmosphere. BSTFA (Davos Chemical) and DDQ (Simafex) were used as received. Electrochemistry was conducted using a 410 potentiostatic controller and 640 digital coulombmeter both from The Electrosynthesis Co. HPLC was performed using a Dupont RX column (4.6 × 250 mm) and 50:50 CH_3CN/0.02 M aqueous H_3PO_4 as eluent at a flow rate of 1.5 mL/min. UV spectra were determined by diode array detection. Microanalyses and HRMS data were provided by the Analytical Research Department and the Department of Natural Product Chemistry, respectively, both of Merck Research Laboratories.

Methyl 3-Oxo-4-azaandrosta-1,5-diene-17β-carboxylate (5). A 4 L beaker equipped with a magnetic stir bar was charged with 3.5 L of methanol, 20.0 g of methyl 3-oxo-4-azaandrost-1-ene-17β-carboxylate (**3**), and 45 g of lithium trifluoromethanesulfonate. Stainless steel (cathode) and carbon felt (anode) electrodes, each 80 cm^2, were submerged 1 cm apart in the resulting slurry. A potential was applied across the electrodes to maintain a constant current of 200 mA. When the starting material had been consumed, the methanol solution was filtered and concentrated to 750 mL. To the resulting slurry in a 5 L three-neck flask equipped with an overhead stirrer and an addition funnel was added 2800 mL of water. The solid was isolated by filtration washing with with 600 mL of water and heated at 100 °C under vacuum for 16 h to give 17.8 g (89% yield, >99 area % pure by HPLC): mp >240 °C; LC retention time 8.0 min; UV λ_{max} 295 nm; IR (nujol) 3170, 1720, 1680, 1595 cm^{-1}; ^1H NMR ($CDCl_3$, 250.1 MHz) δ 8.00 (s, 1H), 6.72 (d, J = 10.0, 1H), 5.82 (dd, J = 1.2, 10.0, 1H), 5.00 (d, J = 3.1, 1H), 3.68 (s, 3H), 2.38 (t, J = 9.0, 1H), 1.23 (s, 3H), 0.70 (s, 3H); ^{13}C ($CDCl_3$, 62.9 MHz) δ 174.3, 163.8, 148.7, 138.4, 121.0, 106.6, 55.9, 55.0, 51.3, 44.0, 43.9, 38.5, 37.8, 32.3, 29.1, 24.3, 23.6, 22.0, 20.7, 13.5. Anal. Calcd for $C_{20}H_{27}N_1O_3$: C, 72.92; H, 8.26; N, 4.25. Found: C, 72.78; H, 8.50; N, 4.38.

Silylation-Mediated Reaction of Methyl 3-Oxo-4-azaandrosta-1,5-diene-17β-carboxylate (5) with DDQ. To a suspension of **5** (155 mg, 0.5 mmol) in 2.6 mL of toluene were added BSTFA (0.6 mL, 22.5 mmol) and triflic acid (1 μL). The result was cooled to −25 °C, and DDQ (115 mg, 0.5 mmol) was added. The mixture was heated at 60 °C for 8 h, and the solvent was removed to give a brown oil which was dissolved in 5 mL of dichloromethane, adding 0.17 mL of methanol. The solution was filtered and the dichloromethane was replaced by ethyl acetate on a rotary evaporator to give the crystalline product which was isolated by filtration, washed with ethyl acetate, and dried under vacuum to give 135 mg of the adduct **13** (49% yield): mp > 310 °C dec; LC retention time 19.1 min; UV λ_{max} 232, 255, 333 nm; IR (nujol) 3330, 2240, 1725, 1660, 1600 cm^{-1}; ^1H NMR (DMSO-d_6, 399.9 MHz) δ 9.22 (br s, 1H), 6.84 (d, J = 10.0, 1H), 5.74 (dd, J = 10.0, 2.0, 1H), 3.59 (s, 3H), 2.38 (t, J = 9.2, 1H), 1.19 (s, 3H), 0.61 (s, 3H); ^{13}C (DMSO-d_6, 100.6 MHz) δ 173.4, 161.6, 154.5, 147.6, 146.4, 132.3, 130.1, 129.2, 125.6, 121.1, 113.8, 112.6, 105.7, 102.2, 54.4, 54.0, 51.1, 43.4, 43.1, 38.1, 37.0, 31.2, 28.9, 23.8, 23.0, 21.1, 20.0, 13.2. Anal. Calcd for $C_{28}H_{27}Cl_2N_3O_5$: C, 60.44; H, 4.89; N, 7.55. Found: C, 60.13; H, 4.90; N, 7.21.

Representative Procedure for the Dehydrogenation of Δ^5-3-Keto-4-azasteroid. Methyl 3-Oxo-4-azaandrosta-1,5,7-triene-17β-carboxylate (6). A three-neck 500 mL flask equipped with an overhead stirrer, nitrogen inlet, addition funnel, and thermocouple was charged with 300 mL of dichloromethane, and **5** (3.0 g, 9.11 mmol) was added. The resulting solution was cooled to −40 °C and a solution of DDQ (2.48 g, 10.9 mmol) in 40 mL of acetonitrile was added. The reaction mixture was warmed to 20 °C. After 18 h the hydroquinone which had crystallized was removed by filtration and the product was crystallized by displacing the dichloromethane with acetonitrile on a rotary evaporator, isolated by filtration, and dried at 80 °C under vacuum to give 1.97 g of the yellow crystalline product (66% yield): mp > 210 °C dec; LC retention time 10.2 min; UV λ_{max} 225, 292, 340 nm; IR (Nujol) 1720, 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 250.1 MHz) δ 8.30 (s, 1H), 6.64 (d, J = 10.1, 1H), 5.94 (dd, J = 10.0, 1.9, 1H), 5.56 (m, 1H), 5.34 (d, J = 6.1, 1H), 3.70 (s, 3H), 2.48 (t, J = 9.4, 1H), 1.07 (s, 3H), 0.65 (s, 3H); ^{13}C ($CDCl_3$, 62.5 MHz) δ 174.3, 163.0, 147.1, 138.2, 133.7, 120.4, 117.2, 102.2, 54.6, 53.8, 51.4, 44.6, 41.3, 38.1, 37.2, 23.5, 23.3, 21.0, 19.1, 13.3. Anal. Calcd for $C_{20}H_{25}N_1O_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.23; H, 7.52; N, 4.05.

***N*-(1,1-Dimethylethyl)-3-oxo-4-azaandrosta-5,7-diene-17β-carboxamide (16).** The compound was obtained as an off-white crystalline solid in 58% yield: mp > 210 °C dec; LC retention time 7.8 min; UV λ_{max} 307 nm; IR (Nujol) 3420, 3180, 1655 cm^{-1}; ^1H NMR ($CDCl_3$, 250.1 MHz) δ 7.94 (s, 1H), 5.46 (m, 1H), 5.13 (m, 2H), 1.36 (s, 9H), 1.07 (s, 3H), 0.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 171.7, 169.5, 139.7, 136.2, 116.8, 100.6, 57.1, 53.8, 51.1, 45.0, 44.0, 37.6, 34.7, 31.8, 29.0, 28.5, 23.2, 20.7, 15.9, 12.8. Anal. Calcd for $C_{23}H_{34}N_2O_2$: C, 74.56; H, 9.25; N, 7.56. Found: C, 74.68; H, 9.00; N, 7.39.

Methyl 3-Oxo-4-azaandrosta-1,5,7,14-tetraene-17β-carboxylate (17). The reaction was conducted as described for the preparation of **6** with one exception. Following the addition of DDQ, the mixture was warmed to 20 °C and filtered immediately. Extended aging at this point resulted in considerable degradation. The yellow crystalline product was obtained in 49% yield (93% pure by HPLC). Attempts to further purify this material by recrystallization or chromatography were not successful: mp > 200 °C dec; LC retention time 8.5 min; UV λ_{max} 212, 340, 362 nm; IR (Nujol) 3180, 1720, 1672, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 399.9 MHz) δ 7.62 (s, 1H), 6.70 (d, J = 10.0, 1H), 6.28 (dd, J = 6.4, 3.2, 1H), 5.96 (dd, J = 10.0, 2.0, 1H), 5.72 (m, 1H), 5.35 (d, J = 6.2, 1H), 3.73 (s, 3H), 2.82 (m, 2H), 2.46 (m, 2H), 2.27 (dt, J = 12.9, 3.6, 1H), 1.83 (m, 2H), 1.49 (td, J = 12.9, 4.4, 1H), 1.08 (s, 3H), 0.93 (s, 3H); ^{13}C ($CDCl_3$, 100.6 MHz) δ 173.7, 162.7, 146.8, 146.3, 140.4, 126.0, 120.8, 119.4, 118.7, 102.7, 56.7, 51.4, 46.9, 41.6, 38.4, 37.5, 31.6, 19.9, 18.3, 17.6 HRMS MH^+ calcd for $C_{20}H_{24}N_1O_3$ 326.1756, found 326.1758.

Methyl 3-Hydroxy-4-azaestra-1,3,5,7,9-pentaene-17β-Carboxylate (7) by DDQ Oxidation. To a suspension of **6** (163 mg, 0.50 mmol) in 7 mL of toluene at 20 °C were added BSTFA (0.6 mL, 4.5 equiv) and triflic acid (1 μL). After the solid had dissolved to give a yellow solution, DDQ (114 mg, 0.50 mmol) was added. The mixture was heated to 100 °C for 5 h and cooled to 20 °C, and 0.5 mL of methanol was added. The residue from concentration was chromatographed on 40 g of silica gel using 5% methanol in dichloromethane as eluent to give 82 mg of **17** (50% yield) and 27 mg of **7** (24% yield) comparable to material isolated from the air oxidation of **6** (*vide infra*).

Methyl 3-Hydroxy-4-azaestra-1,3,5,7,9-pentaene-17β-carboxylate (7) by Air Oxidation. To a suspension of **6** (82 mg, 0.25 mmol) in 3.5 mL of toluene at 20 °C were added BSTFA (0.3 mL, 4.5 equiv) and triflic acid (1 μL). After the solid had dissolved to give a yellow solution, air (dried using $CaSO_4$) was introduced subsurface. The solution was heated at 100 °C for 5 h and cooled to 20 °C, and 0.3 mL of methanol was added producing crystalline product which was isolated by filtration washing with toluene. Drying at 80 °C afforded 24 mg (31% yield) of **7**: mp > 310 °C dec; LC retention time 7.0 min; UV λ_{max} 223, 237, 286, 340 nm; IR (Nujol) 1710, 1655 cm^{-1}; ^1H NMR ($CDCl_3$, 399.9 MHz) δ 9.41(br s, 1H), 7.98 (d, J = 10.0, 1H), 7.20 (d, J = 8.4, 1H), 7.00 (d, J = 8.4, 1H), 6.68 (d, J = 10.0, 1H), 3.74 (s, 3H), 3.22 (dd, J = 18.1, 7.6, 1H), 3.08 (m, 1H), 2.85 (dd, J = 12.4, 7.6, 1H), 2.63 (t, J = 9.4, 1H), 2.40 (m, 2H), 2.26 (m, 2H), 2.10 (m, 1H), 1.86 (m, 1H), 1.73 (m, 1H), 0.61 (s, 3H); ^{13}C ($CDCl_3$, 100.6 MHz) δ 174.1, 162.4, 137.0, 136.7, 133.7, 132.7, 129.2, 121.3, 117.9, 113.3, 54.1, 51.5, 50.7, 43.8, 35.0, 24.5, 24.4, 24.2, 12.5. HRMS MH^+ calcd for $C_{19}H_{22}N_1O_3$ 312.1600, found 312.1569.

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Supporting Information Available: ^1H NMR spectra for **7** and **17** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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