Products and Mechanisms in the Anodic Oxidation of Solanidine-Type Steroidal Alkaloids

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Anodic oxidation of Δ^4-solaniden-3-one, **2**, 3β-acetoxysolanidin, **5**, and 3β-acetoxy-5α-chlorosolanidin, **6**, were performed in CH_3CN–CH_2Cl_2 (1:1)–tetraethylammonium perchlorate electrolyte solution at platinum using controlled potentials. As a result of two-electron oxidation the corresponding N-22 immonium salts (**2a**, **5a**, and **6a**) and N-16 immonium salts (**2b**, **5b**, and **6b**) were isolated in good yield (75–82%) with a ratio of **a**/**b** products of approximately 1.1. The effect of solution conditions on regioselectivity, e.g., formation of **2a** and **2b**, has been shown to be remarkable. The oxidation of **2** in acetone solution gave **2a** in 95% yield, whereas the oxidation in methylene chloride solution gave **2b** in 95% yield. On the basis of the electroanalytical and preparative results as well as molecular orbital calculations with model compounds the mechanism and regioselectivity of the reaction have been deduced.

Introduction

Potato sprouts represent a convenient starting material for steroid hormone production. They contain steroidal glycoalkaloids possessing solanidine, **1**, as the aglycon part, and several methods[1] for determination and isolation of solanidine directly from potato sprouts have been developed.

Chemical degradation of the indolizidine system of **1**, directed toward a synthesis of progesterone, has been reported.[2,3] However, this process[2,3] gave the desired immonium salt **2a** in only 6% yield, while a "side product", **2b**, was formed in a yield of 39% (Scheme 1).

In addition, an alternative route to solanidine degradation was worked out involving the protection of a 3β-hydroxy 5-ene solanidine system by acetylation and addition of HCl to the 5,6-double bond yielding compound **6** (Scheme 2).[1] It is important to point out that the oxidation of compound **6** with Hg(II) acetate, under various reaction conditions, led to a simultaneous regeneration of the 5,6-double bond, *i.e.*, to the formation of *N*-immonium salts **5a** and **5b**.[1]

The present paper describes the first electrochemical oxidation of compounds **2**, **5**, and **6** in order (i) to optimize reaction conditions for the synthesis of desired N-22 immonium salts, (ii) to prevent a regeneration of 5,6-double bond during the electrochemical oxidation of **6**, and (iii) to explain the regioselectivity of the anodic oxidation.

Results and Discussion

Voltammetry and Coulometry. Cyclic voltammograms of compounds **2**, **5**, and **6** were run at a series of potential scan rates in CH_3CN/CH_2Cl_2 (1:1)–0.1 M Et_4NClO_4 solution at a platinum disk anode. The cyclic voltammograms showed one irreversible wave in the potential range studied. The peak currents in all cases were proportional to the square root of the potential sweep rate (in the range 0.05–2.0 V s^{-1}) indicating that the process is diffusion controlled. The addition of pyridine as a base did not alter the height of the wave but caused the cathodic shift of the peak potential by about 30 mV. The addition of perchloric acid shifted the anodic peak potential of **2** to a more positive value (E_p = 1.38 V *vs* SCE) indicating that the protonated amine moiety is more difficult to be oxidized than the free base. The oxidation peaks were broad ($E_p - E_{p/2} > 85$ mV; see Table 1). Such voltammetric behavior can be presumably explained by faster chemical reaction following electron transfer than the electron transfer itself, so that a totally irreversible wave is observed.[4] The variation of E_p with $\log v$ is about 30 mV per decade, and there is no variation of the peak potential with concentration of the substrates, which point to the occurrence of a fast first-order chemical reaction following the electron transfer.[5] Controlled potential coulometric experiments were performed on a preparative scale at potentials 0.3 V more positive than the peak potentials of **2**, **5**, and **6** at a platinum gauze anode (3 × 5 cm) in CH_3CN/CH_2Cl_2 (1:1)–0.1 M Et_4NClO_4 solution. The electrolyses proceeded smoothly with the consumption of 2.0 F mol^{-1}.

Our observations obtained from cyclic voltammetry and

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(1) Gasi, K. M.; Miljkovic, D. *J. Serb. Chem. Soc.* **1988**, *53*, 165 and references cited therein.

(2) Schreiber, K.; Horstman, C. *Chem. Ber.* **1966**, *99*, 3183.

(3) (a) Tanabe, M.; Bogler, J. W. U.S. Pat. 2911402, 1959. (b) Schramm, G.; Austrian Pat., 208494, 1970. (c) Schloegl, K.; Schramm, G.; Obendorf, W. Austrian Pat., 290024, 1971. (d) Schramm, G. Austrian Pat., 290497, 1970.

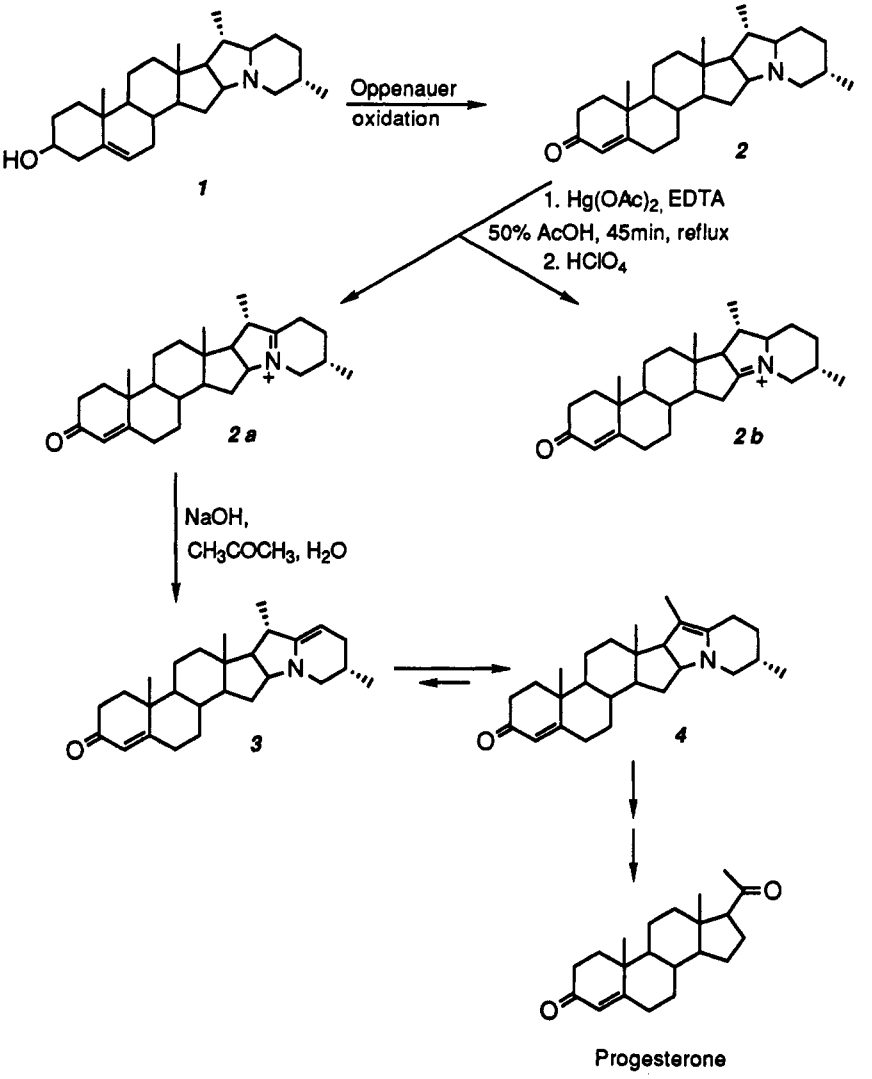
(4) Evans, D. H. *J. Phys. Chem.* **1972**, *76*, 1160.

(5) Nicholson, R. S.; Shain, I. *Anal. Chem.* **1964**, *36*, 706.

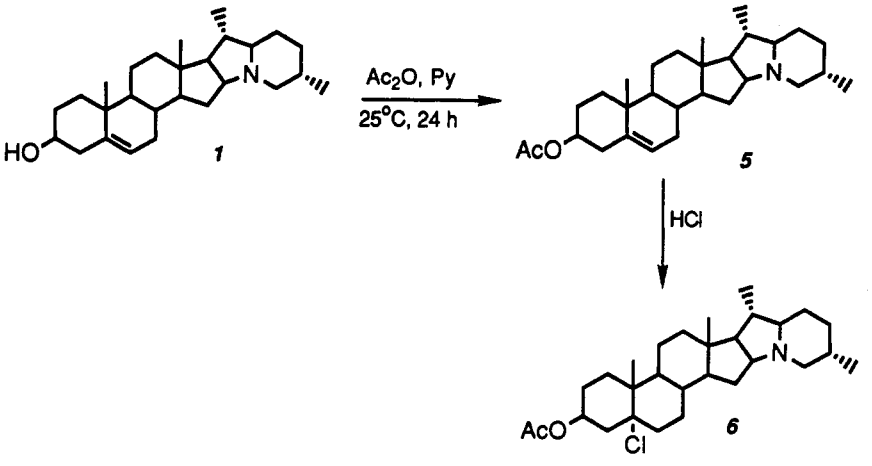
(6) Andrieux, C. P.; Bolcman, C.; Dumas-Bouchiat, J. M.; Hala, F. M.; Saveant, J. M. *J. Electroanal. Chem.* **1980**, *113*, 19.

0022-3263/94/1959-1264$04.50/0

Scheme 1



Scheme 2



controlled potential coulometry are consistent with the fast ECE mechanism for the oxidation of the compounds **2**, **5**, and **6**.

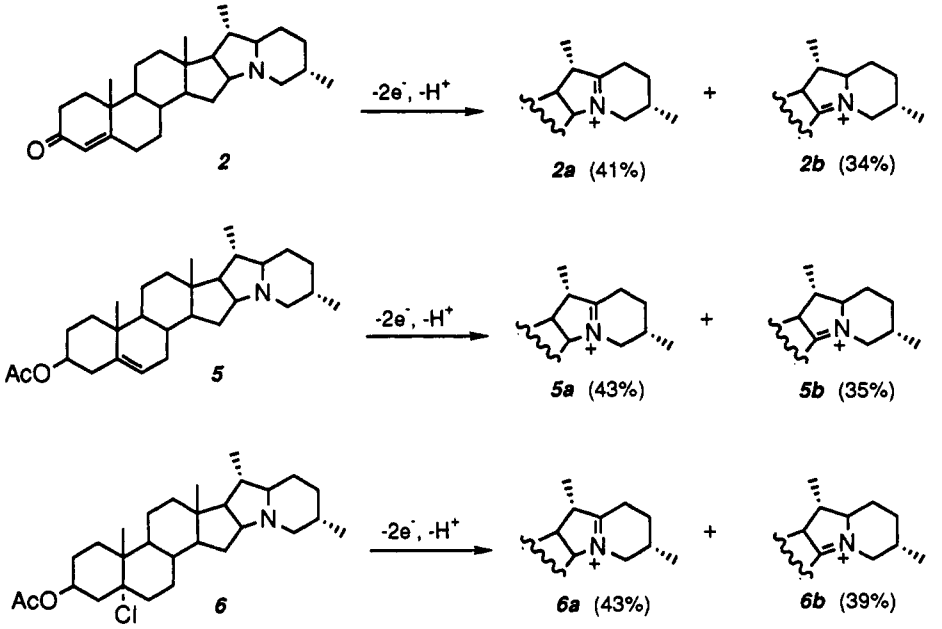
Preparative Electrolysis. Anodic oxidation of compounds **2**, **5**, and **6** in the presence of pyridine as a base was carried out at a platinum gauze anode in CH_3CN/CH_2Cl_2 (1:1)–0.1 M Et_4NClO_4 solution using a divided cell. Coulometry at controlled potential in exhaustive preparative electrolysis showed that the overall electrode reaction was a two electron oxidation. The products N-22 immonium salts (**2a**, **5a**, and **6a**) and N-16 immonium salts

Table 1. Electroanalytical Data[a]

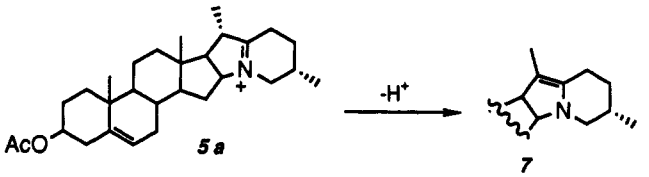
compd	E_p[b] (V *vs* SCE)	$E_p - E_{p/2}$ (mV)	$dE_p/d \log v$ (mV)	$i_p/v^{1/2}$[c] ($\mu AV^{-1/2} s^{1/2}$)	*n*-value[d]
2	0.900	95	32 ± 1	31.62	2.1
5	0.890	90	32 ± 1	34.78	2.2
6	0.895	85	30 ± 1	33.53	2.1

[a] Concentrations of all compounds were 1 mM; CH_3CN/CH_2Cl_2 (1:1); 0.1 M Et_4NClO_4. [b] Peak potentials at 0.1 V s^{-1}. [c] Range of sweep rates: 0.05–2.0 V s^{-1}; Pt anode ($2r$ = 3 mm). [d] Determined value of F mol^{-1} by coulometry in preparative electrolysis at a controlled potential.

Scheme 3



Scheme 4



(**2b**, **5b**, and **6b**) were isolated in good yields (75–82%) as the only two products detected by TLC and HPLC analysis (Scheme 3).

The products were separated by column chromatography, and their spectra were in agreement with the assigned structure. ^{1}H-NMR analysis confirmed the structure of N-22 immonium salt by the presence of a broad singlet at 4.9 ppm corresponding to the proton at C-16 that was absent in the spectra of N-16 immonium salt but showed a peak at 4.2 ppm corresponding to the proton at C-22. The formation of N-22 immonium salts was favored using a direct controlled potential electrolysis (method A, see Experimental Section).

By a careful action of NaOH in acetone on N-22 immonium salt **2a** enamine **3** (Scheme 1) was formed.[3b] Futher isomerization of **3** to **4** was carried out according to the Austrian patents[3c,d] by a modified procedure (see Experimental Section). The reaction occurs presumably through enamine **3**, which is the kinetic product, while on prolonged stirring in an appropriate solvent (acetone or chloroform) enamine **4** predominates as the thermodynamically more stable product. Similarly, N-22 immonium salt **5a** was converted to enamine **7** (Scheme 4).

A small-scale electrolysis of **2** in a different solvent-supporting electrolyte system (Table 2) was performed at a platinum gauze anode (2.5 × 4 cm) and Ni cathode in a divided cell by the constant current electrolysis. The process was monitored by TLC, and after passage of 2.0 F mol^{-1} **2** had disappeared. HPLC analysis of the products provided resolution of both peaks of interest corresponding to **2a** and **2b** within 15 min.

The results of the effect of the solvent on the product distribution after the oxidation of **2** are shown in Table 2.

As can be seen from the results presented in Table 2,

Table 2. Results of the Anodic Oxidation

$$2 \xrightarrow{-2e^- - H^+} 2a + 2b$$

solvent[a]	supporting electrolyte	*n*-value[b]	products (%) 2a	2b
CH_2Cl_2	$NaClO_4$	2.05	traces	95
CH_3CN–CH_2Cl_2 (7:3)	Et_4NClO_4	2.2	42	58
CH_3COCH_3–CH_2Cl_2 (6:4)	$LiClO_4$	2.15	70	10
CH_3COCH_3–CH_2Cl_2 (1:1)	Et_4NClO_4	2.2	90	5
CH_3COCH_3	Et_4NClO_4	2.2	95	traces

the effect of solution conditions on regioselectivity, *e.g.*, formation of N-immonium **2a** and **2b**, is quite remarkable. By carrying out the electrochemical oxidation in acetone one can obtain the desired product **2a** in a high yield. This was proved by performing a preparative oxidation of **2** in which the products **2a** was isolated in 82% yield (method B). An efficient synthesis of "side" product **2b** by carrying out the oxidation in methylene chloride solution is also possible.

Mechanistic Rationalization. The most likely mechanism of the oxidation of **2**, which would fit the observed electroanalytical and preparative results, can be described as in Scheme 5.

Oxidation of **2** is initiated by electron transfer leading to the formation of radical cation, **2**$^{\cdot+}$, (E step). The radical cation is deprotonated giving the radical **2a**$^{\cdot}$ centered at C 22 or **2b**$^{\cdot}$ centered at C 16 (C step). The radical is further oxidized at the applied potential yielding the products **2a** or **2b** (E step). The deprotonation of radical cation **2**$^{\cdot+}$ seems to be a key step for regioselective transformation of **2**. The relative rate of the deprotonation of the proton at C-22 or C-16 is probably determined by the nature of the base (pyridine or solvent) under different solution conditions. Namely, the radical cation **2**$^{\cdot+}$ prefentially deprotonates to **2a**$^{\cdot}$ in acetone (*e.g.*, $k_a \gg k_b$) but gives **2b**$^{\cdot}$ in methylene chloride ($k_b \gg k_a$).

In order to explain our experimental results we have carried out molecular-orbital calculations of 3(*S*),7(*S*)-dimethyl-1,2-cyclopentanoindolizidine **2** used as a model compound. Theoretical self-consistent field calculations were carried out for **2**, radical cation **2**$^{\cdot+}$, radicals **2a**$^{\cdot}$ and

Scheme 5

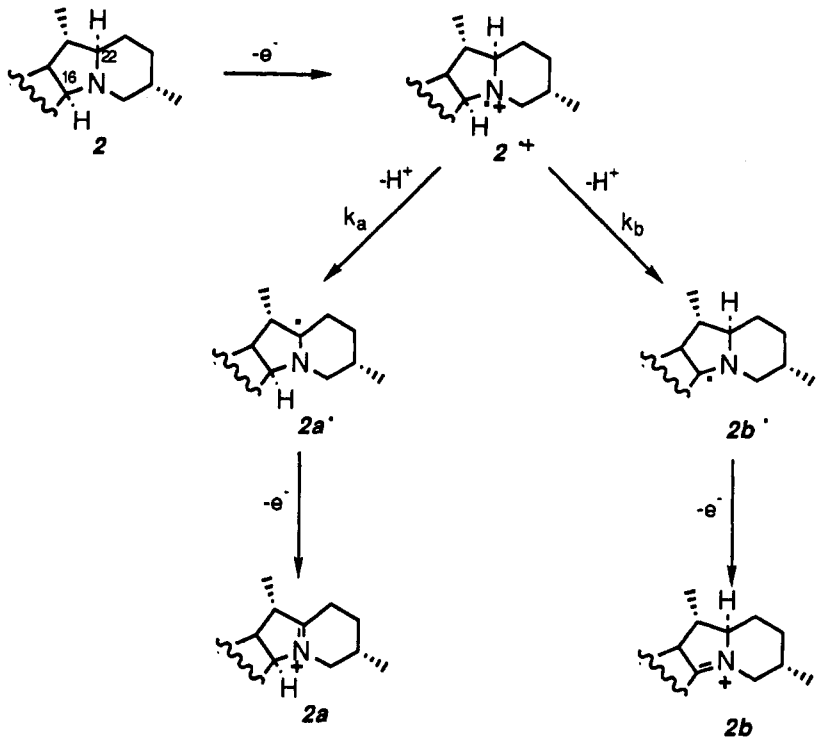
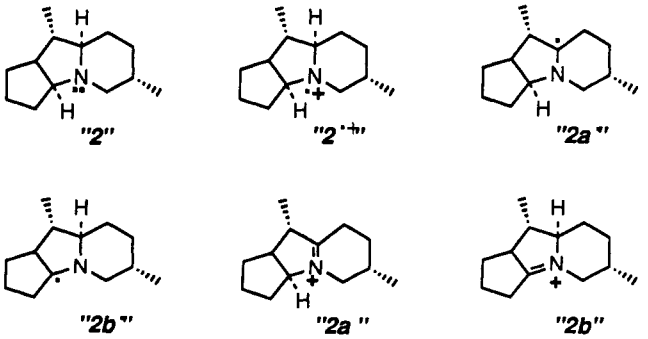


Table 3. Heats of Formation and Ionization Potentials of 3(*S*),7(*S*)-Dimethyl-2,3-cyclopentanoindolizidine 2 and Its Derivatives Calculated by MNDO-PM3 Method

molecule	ΔH_f/kcal mol^{-1}	IP/eV
2	−40.512	8.887
2$^{\cdot+}$	134.313	15.419
2a$^{\cdot}$	−20.594	7.467
2b$^{\cdot}$	−15.689	7.437
2a	119.789	14.859
2b	125.630	15.152

2b$^{\cdot}$, and immonium ions derived from it (**2a** and **2b**). Calculations were performed using the all-valence electron approximation by the MNDO-PM3 method[7] included in program MOPAC.[8] Geometry for all the molecules (including radicals and ions) was obtained on force field minima in vacuum according PM3 method.

Since HOMO levels and ionization potentials can be correlated with electrochemical oxidation potentials,[9] some data on molecules and species **2**, **2**$^{\cdot+}$, **2a**$^{\cdot}$, **2b**$^{\cdot}$, **2a**,and **2b** are given in Table 3.



The distribution of electron densities for electrons in highest MO of calculated molecules and species is given in Figure 1. In **2** the HOMO is essentially a pure lone pair orbital on nitrogen, and the single occupied orbital (SOMO) in **2**$^{\cdot+}$ is broadly similar to it. SOMO orbitals on **2a**$^{\cdot}$ and **2b**$^{\cdot}$ resemble the antibonding π-orbital of the compounds **2a** and **2b**, respectively.

The results obtained by molecular-orbital calculations are in accordance with the postulated ECE mechanism of the anodic oxidation of **2**, **5**, and **6**. Namely, it is reasonable to assume that the primary process is the electron transfer from **2** giving radical cation **2**$^{\cdot+}$. Subsequent prototropic exchange with base produces intermediate radicals **2a**$^{\cdot}$ and **2b**$^{\cdot}$ being more easily oxidized (IP approximately 7.4 eV) than the starting compound **2** (IP for **2** = 8.887 eV). The alternative EEC mechanism is not likely to occur due to the very high oxidation potential of radical cation **2**$^{\cdot+}$ (IP for **2**$^{\cdot+}$ = 15.419 eV).

Inspection of bicentric energy terms for **2**$^{\cdot+}$ shows a considerable difference in bond energies for H–C-22 and H–C-16 bonds, 12.306 and 12.436 eV, respectively, which means that H–C-22 breaks more easily. That will give rise to more stable intermediate **2a**$^{\cdot}$ and more stable product **2a**, as can be seen in Table 3.

The experimentally found preference for the formation of **2b** in electrochemical oxidation of **2** in methylene chloride can be explained by steric hinderance. In Figure 2 is given the van der Waals surface for **2**$^{\cdot+}$.

It is obvious that the hydrogen on C-22 is more sterically hindered than the one on C-16. In methylene chloride the single base available for the proton abstraction from **2**$^{\cdot+}$ is pyridine. It can face considerable steric obstruction approaching the C-22 hydrogen, due to double substitution on nitrogen. The abstraction of the C-16 hydrogen appears to be more feasible. However, in acetone solvent itself can act as a base. Oxygen is singly substituted, behaves as a less voluminous and very weak base, and preferentially takes the C-22 hydrogen, which is more weakly bonded. The steric obstructions for acetone oxygen approach are less severe than for pyridine nitrogen.

However, one has to bear in mind that the anodic oxidation of **2**, as well as **5** and **6**, is occurring through an

(7) Stewart, J. J. *J. Comput. Chem.* **1989**, *10*, 221.
(8) Stewart, J. J. *A General Molecular Orbital Package, (Version 6.01)*, QCPE no. 455.
(9) Yoshida, J.; Itoh, M.; Matsumaga, S.; Isoe, S. *J. Org. Chem.* **1992**, *57*, 4877 and references cited therein.

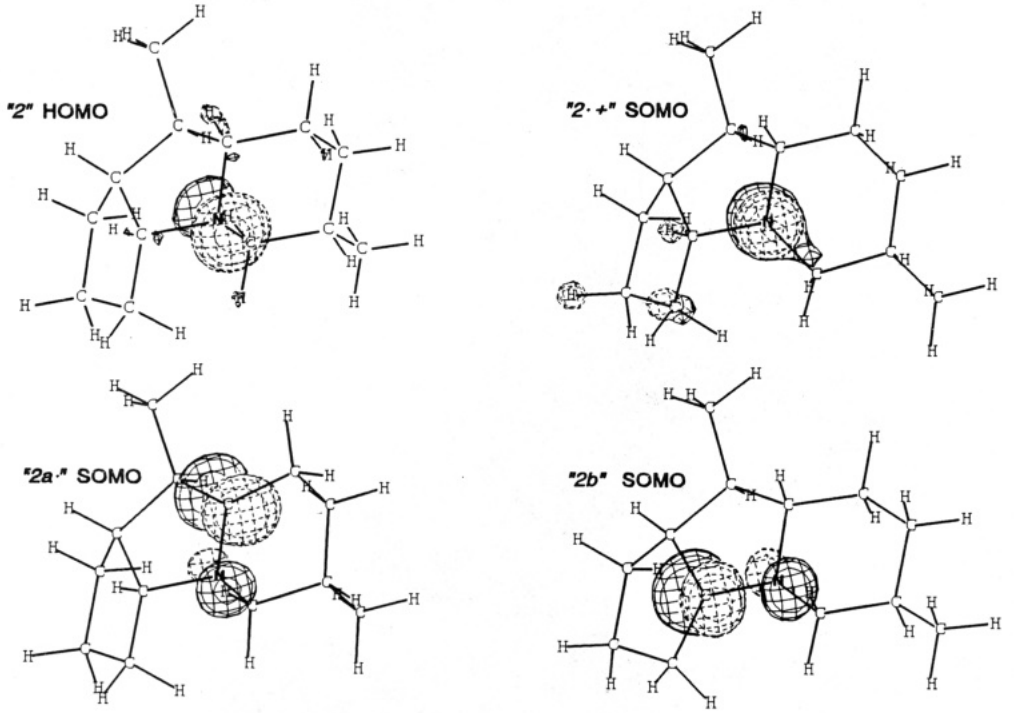


Figure 1. HOMO (SOMO for radicals) for model compound **2** and radicals derived from it.

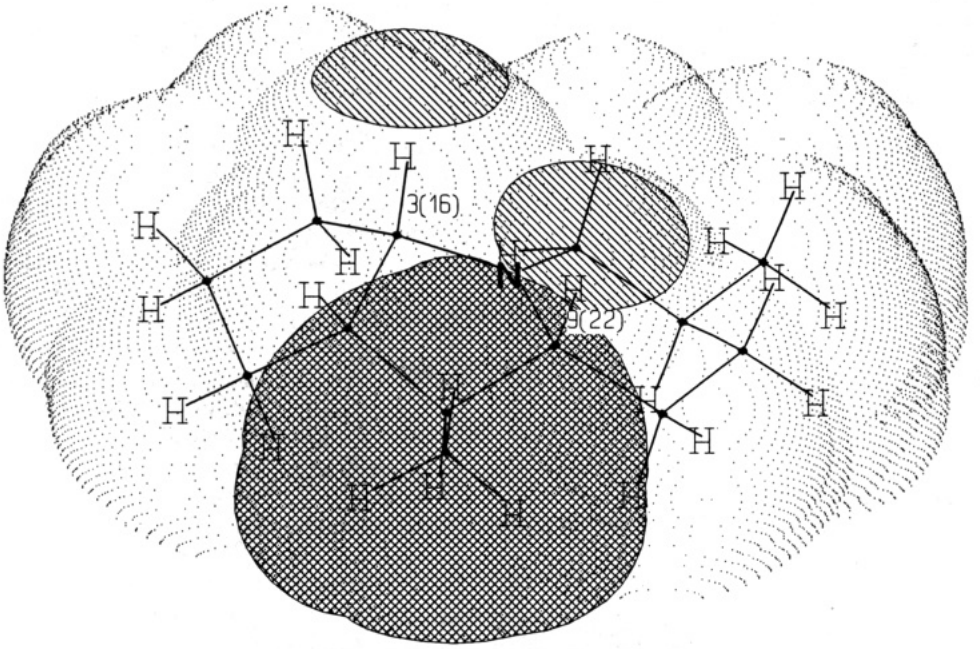


Figure 2. van der Waals surface of 3(*S*),7(*S*)-dimethyl-2,3-cyclopentanoindolizine. Dark area is the C(3) methyl group (corresponding the C(20) methyl group in solanidine). Slightly darkened area are calots of the angular H atoms.

ECE mechanism and that the liberated protons create more acidic media in the reaction layer adhering to the anode than in the homogenous solution. One could propose that the formed radical cation $\mathbf{2}^{\cdot+}$ exists in the fast equilibrium with corresponding radicals $\mathbf{2a}^{\cdot}$ and $\mathbf{2b}^{\cdot}$ due to high concentration of protons in diffusion layer:

$$\mathbf{2a}^{\cdot} + H^+ \rightleftharpoons \mathbf{2}^{\cdot+} \rightleftharpoons \mathbf{2b}^{\cdot} + H^+$$

Intermediate radical $\mathbf{2b}^{\cdot}$ is more easily formed due to less steric hinderance, but it might be more easily subjected to fast reprotonation, which could be more efficient than for the more stable radical $\mathbf{2a}^{\cdot}$. It means that $\mathbf{2b}^{\cdot}$ has a much shorter lifetime and, therefore, its second electron transfer is less probable. The overall result is that thermodynamically more stable $\mathbf{2a}^{\cdot}$ is oxidized at a rate comparable to $\mathbf{2b}^{\cdot}$ because their equilibrium concentrations are not very different.

In a summary, it seems that the formation of **2b** is under kinetic control, while the formation of **2a** is under thermodynamic control when the reaction is occurring through deprotonation of $\mathbf{2}^{\cdot+}$ with pyridine as a base. However, acetone as a much weaker base presumably deprotonates more acidic H–C-22 leading to $\mathbf{2a}^{\cdot}$ which is oxidized at the applied potential giving rise to **2a** in high yield. Another approach to the rationalization of the

problem of discrepancy between the product distribution involves the possible consequences of the adsorption of the intermediates so that one of the protons is more available for the deprotonation by base. It is important to note that a similar kind of explanation of the mean factors (nature of the base and/or adsorption) were considered in the studies on the anodic methoxylation of *N,N*-dimethylbenzylamine.[10-13]

In conclusion, we can say that the anodic oxidation of solanidine-type steroidal alkaloids gave rise to the high yield of desired N-22 immonium salts and the regeneration of the 5,6-double bond during the anodic oxidation of substrate **6** was prevented.

Experimental Section

Materials and Apparatus. Acetonitrile (Merck) was purified by refluxing over potassium permanganate for 1 h, followed by distillation over P_2O_5. Methylene chloride (BDH) was shaken with concentrated H_2SO_4 and after being washed with water and diluted sodium bicarbonate it was dried ($CaCl_2$) and distilled from calcium hydroxide. Acetone (Merck) was dried over anhydrous calcium sulfate for 2 days and then distilled from fresh calcium sulfate. The supporting electrolytes (Et_4NClO_4, $NaClO_4$, Bu_4NPF_6) were crystallized from water and dried under vacuum over P_2O_5. $LiClO_4$ (Fluka) was used as such. The apparatus and cells for voltammetry, coulometry, and preparative electrolysis have been described earlier.

IR spectra were recorded with a Perkin-Elmer 457 spectrometer. NMR spectra were recorded with a Brucker WP 250 SY instrument; chemical shifts are given in ppm; the symbols s, d, t, and m denote singlet, doublet, triplet, and multiplet, respectively. Mass spectra were taken with Varian CH-5 and Varian MAT 311A spectrometers. Melting points were determined with a Büchi SMP-20 apparatus and are not corrected. HPLC analysis was performed with a Varian Vista 5500 equipped with a UV-200 detector and integrator Varian 440 using microcolmn MCH-5 N CAP (15 cm × 4 mm) with eluant CH_3CN–H_2O (8:2); 0.3 mL/min at 210 nm.

General Procedure for Direct Controlled Potential Oxidation of 2, 5, and 6 (Method A). To the anodic compartment of the divided cell with a Pt gauze anode (3 × 5 cm) and Ni cathode filled with 0.1 M solution of Et_4NClO_4 in CH_3CN–CH_2Cl_2 (1:1) (100 mL) were added the substrate (1 mmol) and pyridine as a base (200 μL). The potential was maintained at a fixed value (E = 1.2 V *vs* SCE) with initial currents of 200–260 mA generally. Electrolysis was usually discontinued when the current dropped to 10 mA. The solution was evaporated to ca. 10 mL. Into this mixture was added 20 mL of water containing a few drops of $HClO_4$. The precipitated products were isolated by filtration, washed with ether, and dried. The products were separated by column chromatography using silica gel or Al_2O_3 (50 g) with benzene–methanol (10:1) as an eluent. N-16 immonium perchlorates **2b** (34%, mp 147–151 °C), **5b** (35%, mp 204–206 °C), and **6b** (39%, mp 189–190 °C) were isolated as the first fraction and N-22 immonium salts **2a** (41%, mp 272–275 °C (lit.[3] mp 273–287 °C)), **5a** (43%, mp 271°C (lit.[3] mp 270–278 °C)), and **6a** (43%, mp 165–168 °C) as a second fraction.

2a: IR (KBr) 1675, 1670, 1615, 1090, 625 cm^{-1}; NMR ($CDCl_3$) 0.71 (s, 3H), 1.11 (d, 3H), 1.18 (s, 3H), 1.45 (d, 3H), 4.98 (d, 1H), 5.72 (s, 1H); MS 394 ($M^+ - ClO_4$; 100.00) 379 (6.66), 154 (16.00), 135 (23.00), 107 (14.00). Anal. Calcd for $C_{27}H_{40}ClNO_5$: C, 65.64; H, 8.16; N, 2.84. Found: C, 65.64; H, 8.35; N, 2.63.

2b: IR (KBr) 1710, 1665, 1615, 1090, 625 cm^{-1}; NMR ($CDCl_3$) 0.84 (s, 3H), 1.03 (d, 3H), 1.21 (s, 3H), 1.23 (d, 3H), 3.97 (d, 2H), 4.26 (s, 1H), 5.73 (s, 1H). Anal. Calcd for $C_{27}H_{40}ClNO_5$: C, 65.64; H, 8.16; N, 2.84. Found: C, 65.39; H, 8.25; N, 2.78.

5a: IR (KBr) 1730, 1675, 1255, 1090, 1035, 625 cm^{-1}; NMR ($CDCl_3$) 0.68 (s, 3H), 1.00 (s, 3H), 1.10 (d, 3H), 1.45 (d, 3H), 2.05 (s, 3H), 4.59 (m, 1H), 4.98 (d, 1H), 5.35 (d, 1H); MS 324 (9.00), 257 (18.00), 193 (19.00), 149 (100), 105 (26.00). Anal. Calcd for $C_{29}H_{44}ClNO_6$: C, 64.72; H, 8.24; N, 2.60. Found: C, 64.66; H, 8.20; N, 2.60.

5b: IR (KBr) 1730, 1715, 1255, 1090, 625 cm^{-1}; NMR ($CDCl_3$) 0.80 (s, 3H), 1.03 (d, 3H), 1.20 (d, 3H), 2.04 (s, 3H), 3.15 (d, 1H), 4.27 (m, 1H), 4.59 (m, 1H), 5.35 (d, 1H); MS 364 (1.5), 324 (36.00), 149 (38.00), 84 (44.00), 57 (46.00). Anal. Calcd for $C_{29}H_{44}ClNO_6$: C, 64.72; H, 8.24; N, 2.60. Found: C, 64.75; H, 8.21; N, 2.58%.

6a: IR (Kbr) 1733, 1680, 1461, 1097, 624 cm^{-1}; NMR ($CDCl_3$) 0.82 (s, 3H), 1.05 (s, 3H), 1.13 (d, 3H), 1.45 (d, 3H), 4.98 (d, 1H), 5.38 (s, 1H). Anal. Calcd for $C_{29}H_{45}Cl_2NO_6$: C, 60.62; H, 7.89; N, 2.44. Found: C, 60.58; H, 7.67; N, 2.23.

6b: IR (Kbr) 1735, 1636, 1458, 1092, 624 cm^{-1}; NMR ($CDCl_3$) 0.80 (s, 3H), 1.05 (s, 3H), 1.20 (s, 3H), 1.45 (d, 3H), 3.95 (m, 1H), 4.27 (m, 1H), 4.33 (m, 1H), 5.37 (d, 1H); MS 439 (3.00), 438 (4.00), 420 (2.90), 379 (5.60), 283 (8.00), 204 (5.00), 162 (6.00), 150 (21.50). Anal. Calcd for $C_{29}H_{45}Cl_2NO_6$: C, 60.62; H, 7.89; N, 2.44. Found: C, 60.82; H, 7.75; N 2.29.

Procedure for Constant Current Oxidation of 2 in Acetone as Solvent (Method B). To the anodic compartment of the divided cell with a Pt gauze anode (3 × 5 cm) and Ni cathode filled with 0.1 M solution of Et_4NClO_4 in acetone (100 mL) were added **2** (400 mg, 1.00 mmol), and pyridine as base (200 μL). The current was maintained at a constant value (I = 100 mA), and electrolysis proceeded for 40 min. The solution was evaporated to ca. 10 mL. Into this mixture was added 80 mL of water containing a few drops of $HClO_4$. The precipitated product was isolated by filtration, washed with ether and dried. After the recrystallization from $CHCl_3$–ether (1:3), the product **2a** (82%) was obtained as an analytically pure sample.

General Procedure for the Synthesis of 20(22)-Enamines. N-22 Immonium salts (**2a** or **5a**; 100 mg) were dissolved in a hot mixture (40 °C) of acetone (20 mL) and water (10 mL). Into this mixture was added 2 mL of a 30% solution of NaOH. After 15 min the mixture was cooled to room temperature, and 50 mL of water was added. The precipitated product (22(23)-enamines) was isolated by filtration. The crude product was dissolved in 20 mL of ether with a few drops of AcOH and then in the dark room bubbled with nitrogen (30 min), diluted with water (ca. 20 mL), neutralized with $NaHCO_3$ and extracted with ether. After the combined ether extract was dried with anhydrous Na_2SO_4 and ether was removed in vacuum, the crude products **4** (mp 158–159 °C) and **7** (mp 147–151 °C) were obtained (92–95%).

4: IR (KBr) 3500–3300, 2920, 1675, 1450, 1380, 1230, 1020, 865 cm^{-1}; NMR ($CDCl_3$) 0.60 (s, 3H), 0.82 (d, 3H), 1.08 (s, 3H), 1.50 (s, 3H), 5.65 (s, 1H); MS 393 (5.00), 162 (100), 149 (12.00), 134 (5.00), 79 (4.00), 55 (5.00). Anal. Calcd for $C_{27}H_{39}NO$: C, 82.39; H, 9.99; N, 3.56. Found: C, 82.08; H, 10.04; N, 3.12.

7: IR (KBr) 3500–3300, 2900, 1730, 1670, 1450, 1370, 1240, 1135, 1025 cm^{-1}; NMR ($CDCl_3$) 0.63 (s, 3H), 0.87 (d, 3H), 1.02 (s, 3H), 1.58 (s, 3H), 2.03 (s, 3H), 4.50-4.70 (m, 1H), 5.40 (d, 1H). Anal. Calcd for $C_{29}H_{42}NO$: C, 82.80; H, 10.06; N, 3.33. Found: C, 82.66; H, 9.95; N, 3.07.

3β-Acetoxy-5α-chlorosolanidane (6). 3β-Acetoxy-5-solanidene (7.50 g, 17 mmol) was dissolved in a mixture of $CHCl_3$ (40 mL) and glacial AcOH (40 mL). Through this solution, cooled at 0 °C, was bubbled dry gaseous HCl until saturation (3–5 h). The reaction mixture was kept for 7 days in a refrigerator at 4 °C and then diluted with water (ca. 300 mL), neutralized with $NaHCO_3$, and extracted with chloroform (3–4 × 50 mL). After the combined chloroform extract was dried with anhydrous Na_2SO_4 and chloroform was removed in vacuum, the crude product **6** was obtained (96–99%). Chromatography on an aluminum oxide column (750 g, petroleum ether:acetone = 10:1) and recrystallization from AcOEt afforded pure compound **6** in a yield of 90%, mp 304–307 °C.

7: IR (KBr) 1740, 1450, 1370, 1260, 1245, 1030 cm^{-1}; NMR ($CDCl_3$) 0.75 (s, 3H), 0.85 (d, 3H), 0.95 (d, 3H), 1.10 (s, 3H), 2.05 (s, 3H), 5.35 (m, 1H); MS 475 (M^+, 1.80), 439 (14.00), 424 (6.00), 378 (11.00), 204 (31.00), 150 (100). Anal. Calcd for $C_{29}H_{43}ClNO_2$: C, 73.62; H, 9.16; N, 2.96. Found: C, 73.34; H, 9.07; N, 3.00.

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(10) Weinberg, N. L.; Brown, E. A. *J. Org. Chem.* **1966**, *31*, 4054.
(11) Smith, P. J.; Mann, C. K. *J. Org. Chem.* **1968**, *33*, 316.
(12) Weinberg, N. L. *J. Org. Chem.* **1968**, *33*, 4326.
(13) Barry, J. E.; Finkelstein, M.; Mayeda, E. A.; Ross, S. D. *J. Org. Chem.* **1974**, *39*, 2695.
(14) Gunic, E.; Tabakovic, I. *J. Org. Chem.* **1988**, *53*, 5081.