Chemical and Electrochemical Reduction of Pyrido-*as*-triazines[1]

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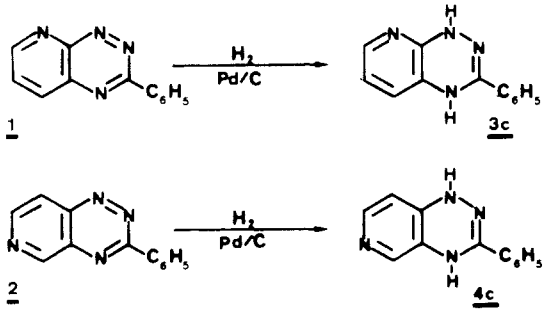
The catalytic hydrogenation of 3-phenylpyrido[3,2-*e*]-*as*-triazine (**1**) and of 3-phenylpyrido[3,4-*e*]-*as*-triazine (**2**) leads to the corresponding 1,4-dihydro derivatives **3c** and **4c**. The structures of these compounds were established by ^{1}H NMR using the nuclear Overhauser effect and long-range coupling constants. Reduction by $LiAlH_4$ gives the 5,6,7,8-tetrahydro derivative of **1** and the 4,5,6,10-tetrahydro derivative of **2**; the conformation of the latter compound has been established. In aqueous methanol, **1** and **2** are electrochemically reduced into **3c** and **4c**, respectively; the same products are obtained in acetonitrile in the presence of phenol. The electrochemical reduction of **2** in acetonitrile in the presence of acetic anhydride leads to a mixture of 1,4-diacetyl-1,4-dihydro and 1,2-diacetyl-1,2-dihydro compounds. These results are compared with those obtained in the reduction of other azanaphthalenes.

The chemical and electrochemical reductions of several series of azanaphthalenes (N heterocycles with two six-membered fused rings) have been reported. Examples include quinoxalines,[2,3] cinnolines,[4-6] phthalazines,[7,8] quinazolines,[9,10] pyridopyrazines,[9,11-14] and benzotriazines.[15,16] Although several papers have appeared dealing with the synthesis of pyridotriazines,[17-23] their reduction has never been investigated. We now report the results obtained by hydrogenation, $LiAlH_4$ reduction, and electrochemical reduction of 3-phenylpyrido[3,2-*e*]-*as*-triazine (**1**) and of 3-phenylpyrido[3,4-*e*]-*as*-triazine (**2**), which are representative examples of both series. The results will be compared with those obtained with other types of azanaphthalenes.

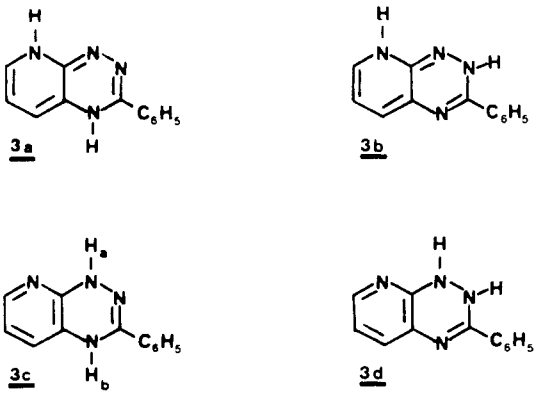
Hydrogenation. In the presence of Pd/C, hydrogenation of **1** and **2** leads to the dihydro derivatives **3c** and **4c**, the structures of which were determined by NMR (Table I).



The reduction product of **1** has two amino protons which are readily exchanged by addition of D_2O, so that the four isomeric structures **3a-d** have to be considered.

The resonances of H_5, H_6, and H_7 can be unambiguously assigned since their chemical shifts follow the same sequence as those of pyridine ($\delta_\alpha > \delta_\gamma > \delta_\beta$), and the coupling constants $^3J_{H5H6}$, $^3J_{H6H7}$, and $^4J_{H5H7}$ have values close to those reported for pyridine ($^3J_{\alpha\beta}$ = 5.5 Hz, $^3J_{\beta\gamma}$ = 7.6 Hz, $^4J_{\alpha\gamma}$ = 1.9 Hz).[24]

In dimethyl-d_6 sulfoxide solution, the two NH signals are far enough apart to be selectively irradiated. Irradiation of NH_b (δ 8.24) does not suppress the 0.5-Hz coupling constant observed on the H_5 signal but results in a 14% NOE enhancement of this H_5 signal. This NOE indicates



that H_b is bonded to N_4 and thus excludes structures **3b** and **3d**.

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Table I. NMR Data[a,b] for 3c and 4c

compd	chemical shift						
	H_5	H_6	H_7	H_8	H_a[c]	H_b[c]	C_6H_5
3c	6.51 (ddd, $^3J_{H_5H_6}$ = 7.4)	6.35 (dd, $^3J_{H_6H_7}$ = 5.0)	7.27 (dd, $^4J_{H_5H_7}$ = 1.7)		8.35 (s, $^5J_{H_5H_a}$ = 0.5)	8.24 (s)	~7.42 (m, 3 H), ~7.68 (m, 2 H)
4c	7.43 (dd, $^5J_{H_5H_8}$ = 0.3)		7.63 (d, $^3J_{H_7H_8}$ = 4.9)	6.03$_5$ (dd)	8.30 (s, $^5J_{H_5H_a}$ ≈ 0.3)	8.08$_7$ ($^5J_{H_8H_b}$ ≈ 0.25)	~7.45 (m, 3 H), ~7.69 (m, 2 H)

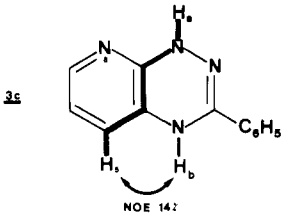
[a] Obtained at 100 MHz, solvent Me_2SO-d_6. [b] δ values in parts per million relative to internal Me_4Si; J values are in hertz. [c] Broad, exchanges with D_2O.

Table II. NMR Data[a,b] for 8

solvent	temp, °C	chemical shift							
		H_{5a}	H_{5e}	H_7	H_8	H_{10a}	H_a[c]	H_b[c]	C_6H_5
Me_2SO-d_6	32	3.05 (t, $^2J_{H_{5a}H_{5e}}$ = −11.4)	3.76 (dd, $^3J_{H_{5e}H_{10}}$ = 5.96)	6.65 (d, $^4J_{H_{5a}H_7}$ = 0.5)	4.90 (d, $^3J_{H_7H_8}$ = 7.2)	4.05 (dd, $^3J_{H_{5a}H_{10}}$ = 11.8)	10.0 (s)	6.17 (s)	~7.83 (m, 2 H), ~7.42 (m, 3 H)
pyridine-d_5–CD_2Cl_2 (80/20 v/v)	−60	3.66 (t, $^2J_{H_{5a}H_{5e}}$ = −11.2)	4.28 (ddd, $^3J_{H_{5e}H_{10}}$ = 5.8, $^3J_{H_{5e}H_6}$ = 3.2)	6.91 (dd, $^3J_{H_6H_7}$ = 5.8)	5.50 (d, $^3J_{H_7H_8}$ = 7.2)	4.69 (dd, $^3J_{H_{5a}H_{10}}$ = 12)	12.0 (s)	7.34 (s)	~7.46 (m, 3 H), ~8.26 (m, 2 H)

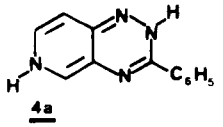
[a] Obtained at 100 MHz. [b] δ values are in parts per million relative to internal Me_4Si; J values are in hertz. [c] Broad exchanges with D_2O.

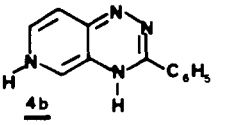
Irradiation of NH_a (δ 8.35) does not produce any detectable NOE enhancement but suppresses the small coupling constant observed on the H_5 signal ($^5J_{H5Ha}$ = 0.5 Hz). This absence of a NOE and the lack of spin–spin coupling between H_7 and H_a expected for **3a** exclude structure **3a**. Only structure **3c** is in agreement with the

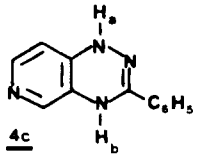


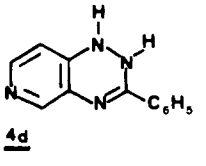
NOE experiments and with the existence of the long-range $^5J_{H5Ha}$ coupling constant, which involves a zig-zag pathway. Such intercyclic $^5J_{HH}$ values have been observed in several heterocycles such as quinoline ($^5J_{H4H8}$ = 0.8 Hz)[25] and quinazoline ($^5J_{H5H8}$ = 0.5 Hz).[26]

The reduction product of **2** also has two amino protons which can be exchanged by addition of D_2O, and the four isomeric structures **4a–d** can be written.



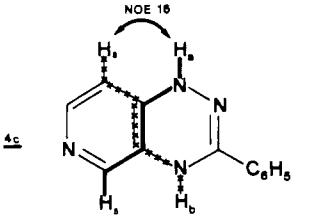






Before deuteration of the amino protons, the H_5 and H_8 signals are broad, thus suggesting unresolved coupling constants. After the H/D exchange these signals become sharp, and a well-resolved $^5J_{H5H8}$ = 0.35 Hz is observed.

The low-field H_5 and H_7 signals partly overlap those of the aromatic protons, so that only the high-field H_8 signal can be used for an NOE experiment. Irradiation of NH_a (δ 8.30) induced a 16% NOE on the H_8 signal. This result indicates that H_a is bonded to N_1 and thus excludes structures **4a** and **4b**.



The existence of unresolved coupling constants is shown by double-resonance experiments, and the method described by Sardella[27] was used to evaluate these couplings. Irradiation of N_1–H_a sharpens the H_5 signal and indicates that $^5J_{H5Ha} \approx 0.3$ Hz. Similarly, irradiation of N–H_b sharpens the H_8 signal and gives $^5J_{H8Hb} \approx 0.25$ Hz. Only structure **4c**, in which the protons H_a/H_5 and H_b/H_8 involve planar zig-zag pathways, can account for these long-range intercyclic coupling constants.

The fact that both **1** and **2** give 1,4-dihydro derivatives shows that the position of the nitrogen atom of the pyridine ring does not influence the reduction. When compared with the results obtained for the hydrogenation of other fused six-membered heterocycles, this result appears unusual; quinoxalines give 1,2,3,4-tetrahydro derivatives[2] as pyrido[2,3-*b*]pyrazines;[11] quinazolines[9] as well as benzotriazines[15] give 1,2-dihydro compounds. Only cinnolines[4] give 1,4-dihydro compounds, but in this case the two hydrogen atoms are bonded to a nitrogen and to a carbon

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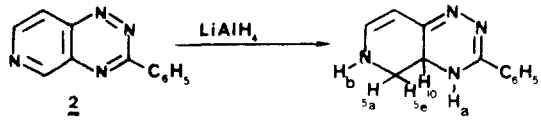
atom. The stability of **3c** and **4c** in solution must also be pointed out: the 1,4-dihydro derivatives obtained through the electrochemical reduction of quinoxalines[3] or of pyridopyrazines[13] easily isomerize into 1,2- or 3,4-dihydro compounds.

Reduction by $LiAlH_4$. The reduction of **1** leads to **5**, in which the pyridine ring is hydrogenated, and the same result is obtained with pyrido[3,2-*e*]-*as*-triazine (**6**).

1 R = C_6H_5 **5** R = C_6H_5
6 R = H **7** R = H

Compounds **2** leads to the unexpected formation of the tetrahydrogenated compound **8**, in which both rings are partially reduced.



2 **8**

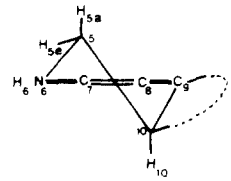
The assignment of the structure **8** rests upon an NMR study (Table II). The proton spectrum of **8** exhibits a low-field AB pattern (H_7/H_8) and a high-field AMX system due to H_{10}, H_{5e}, and H_{5a}, respectively.

Tickling experiments on the AMX system to determine the relative signs of the three coupling constants, indicated that J_{AM} and J_{AX} bear the same sign while J_{AX} and J_{MX} are of opposite signs. Consequently, J_{MX} is a geminal coupling constant ($^2J_{H_{5a}H_{5e}}$) while J_{AM} and J_{AX} are vicinal coupling constants. Moreover, from the magnitude of J_{AX} = 11.8 Hz and J_{AM} = 8 Hz, it was concluded that H_A (H_{10}) and H_X (H_{5a}) are axial–axial while H_M (H_{5e}) is equatorial.

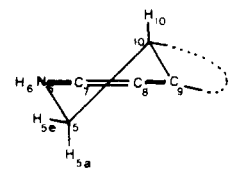
Two broad NH signals are observed at 32 °C (Me_2SO-d_6), but no coupling involving these amino protons is observed, even in the presence of molecular sieves. This absence of coupling is ascribed to a fast chemical exchange, as evidenced by a low-temperature study. At −60 °C (pyridine-d_5–CD_2Cl_2, 80/20 v/v) the resonances of H_7 and H_{5e} exhibit extra couplings, which are suppressed by irradiation of the amino proton H_b at 7.34 ppm: this amino proton is thus bonded to N_6. The lack of coupling between this amino H_6 proton and H_{5a}, even at low temperature, suggests that the dihedral angle H_6–N_6–C_5–H_{5a} is close to 90°.[28]

No coupling involving the low-field amino proton H_a (δ 12) is observed, even at low temperature (−80 °C) so that ^1H NMR alone does not show if this proton is bonded to N_2 or to N_4. However, reduction of the C_{10}–N_4 double bond appears to be more likely on chemical grounds. The structure of **8** is confirmed by its ^{13}C NMR spectrum. It shows eight low-field signals due to sp^2 carbons and two upfield signals corresponding to two sp^3 carbons. Two different conformations, **8a** and **8b**, where H_{10} is in an axial position, can be considered.

The reduction of several azanaphthalenes by $LiAlH_4$ has been investigated, and it is possible to compare the regioselectivity observed in these cases with that obtained in the cases of **1** and **2**. Cinnolines[5] yield 1,2-dihydro and 1,2,3,4-tetrahydro derivatives; 2,3-dimethylquinoxaline



8a



8b

leads exclusively to the *cis*-1,2,3,4-tetrahydro derivative.[2] Pyrido[2,3-*d*]pyridazine yields a mixture of 1,2- and 3,4-dihydro compounds.[14] Pyrido[2,3-*b*]- or -[3,4-*b*]pyrazines yield 1,2,3,4-tetrahydro derivatives.[2,12]

In view of the above results one would expect a reduction of **1** and **2** involving only the triazine ring; in fact, in the case of **1**, only the pyridine ring is reduced, and in the case of **2** both rings are partially reduced in addition to the unexpected bonding of a hydrogen at C_{10}. Contrary to what is observed with pyridopyrazines, the position of the nitrogen atom on the pyridine ring is of prime importance in the orientation of the reduction.

The π electron densities have been determined by Wait and Wesley[29a] using the HMO method; their results indicate that the most basic nitrogen atom is the one in the pyridne ring in all pyrido-*as*-triazines and pyridopyrazines. Recently the CNDO total density ($\sigma + \pi$) values were published for pyrido-*as*-triazine by Dinya et al.[29b] The CNDO results indicate that the pyrido N atom is not the most negative in all cases. For pyrido[2,3-*e*]- and pyrido[3,2-*e*]-*as*-triazines, the largest negative charge is located on the pyrido N atom, but for the [3,4-*e*] and [4,3-*e*] compounds the largest negative charge is on the N_4 atom of the *as*-triazine ring.

At the present time we have no explanation for the different behavior of **1** and **2** in chemical reduction.

Electrochemical Reduction. Aqueous–Organic Medium (50% Aqueous CH_3OH). Between pH 2 and 13, **1** and **2** present a 2-F cathodic wave corresponding to reduction to 1,4-dihydro derivatives. This is confirmed by the electrolysis of dilute solutions (pH 7; E = −0.6 V, c = 10^{-3} M) which give quantitatively **3c** and **4c**.[30] both of these compounds show a 2-F anodic wave with a half-wave potential near those of **1** and **2**. The $E_{1/2} = f(pH)$ plots show two linear parts; thus, in the case of **1** at pH <4.4, $E_{1/2}$ = 0.28 − 0.090pH, and pH >4.4, $E_{1/2}$ = 0.15 − 0.060pH. For **2** at pH <7.3, $E_{1/2}$ = 0.37 − 0.085pH, and at pH >7.3, $E_{1/2}$ = 0.18 − 0.059pH. The intersections of the straight lines correspond to the pK values of **3c** and **4c** as verified by spectrophotometry: one finds pK = 4.42 ± 0.05 for **1** and pK = 7.28 ± 0.05 for **2**. The reduction schemes are shown in eq 1–4.

$$1 + 2e^- + 3H^+ \rightleftarrows (\mathbf{3c})H^+ \text{ (pH <4.4)} \quad (1)$$

$$1 + 2e^- + 2H^+ \rightleftarrows \mathbf{3c} \text{ (pH >4.4)} \quad (2)$$

$$2 + 2e^- + 3H^+ \rightleftarrows (\mathbf{4c})H^+ \text{ (pH <7.3)} \quad (3)$$

$$2 + 2e^- + 2H^+ \rightleftarrows \mathbf{4c} \text{ (pH >7.3)} \quad (4)$$

The polarograms of pyrido[3,4-*e*]-*as*-triazines with other groups at position 3 (R = 2-furyl, 2-thienyl, 2-pyrrolyl, and 2-indolyl) are similar to those of **2**; in all cases the plot of $E_{1/2}$ vs. pH gives two straight lines intersecting at pH 7.3 with slopes similar to those of **2**. For example, when R =

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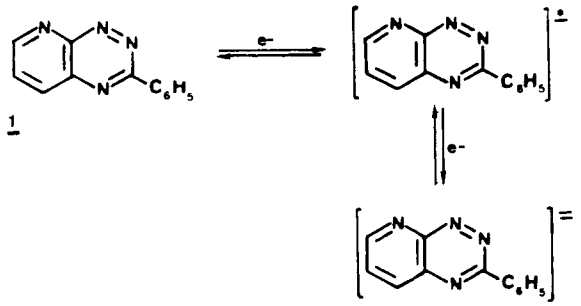
(30) The electrolyzed solutions show the same UV spectra and the same polarograms as 10^{-3} M solutions of **3c** and **4c**.

Scheme I

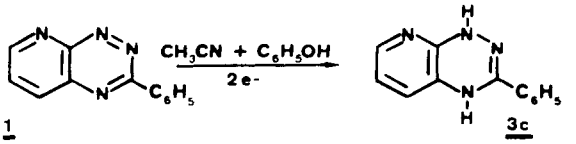


2-thienyl and R = 2-indolyl, one obtains $E_{1/2}$ = 0.17 − 0.059pH (pH >7.3) and $E_{1/2}$ = 0.36 − 0.085pH (pH <7.3). This shows that the reducibility of the heterocycles and the pK values of the 1,4-dihydro derivatives are influenced very little by the nature of the groups in the 3-position.

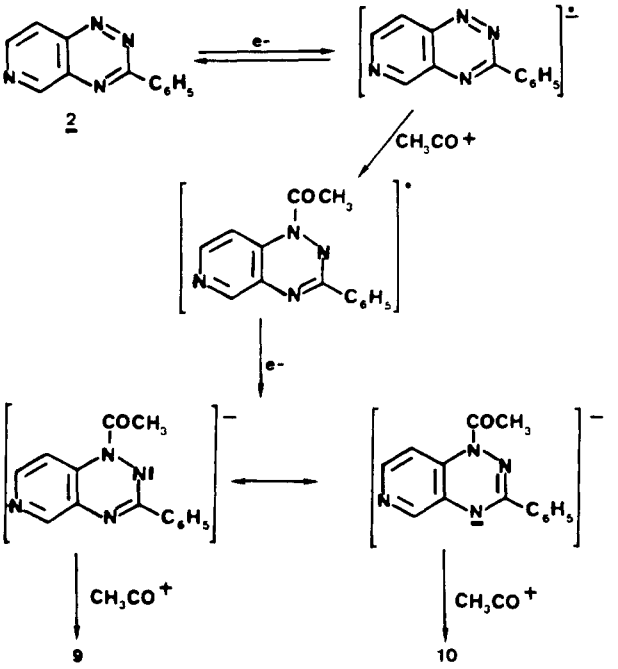
The formation of 1,4-dihydro derivatives from 1 and 2 is similar to the results obtained with quinoxalines,[3] benzotriazines,[16] and pyridopyrazines.[13] As expected, 1 and 2 are more easily reduced than the above compounds: in the azanaphthalene series the ease of reduction increases with the number of nitrogen atoms.[31] The 1,4-dihydro derivatives **3c** and **4c** can be isolated as they are less easily oxidized than the 1,4-dihydroquinoxalines or pyridopyrazines. This ease of oxidation can be related to the difference of $E_{1/2}$ at pH 7 between the wave of oxygen (−0.1 V) and that of the anodic wave of the 1,4-dihydro derivative. When $\Delta E_{1/2}$ is more negative than −0.3 V, the 1,4-dihydro compounds are very readily oxidized: e.g., 1,4-dihydro-2,3-diphenylquinoxaline ($E_{1/2}$ = −0.67 V),[3] 1,4-dihydro-2,3-diphenylpyrido[2,3-*b*]pyrazine ($E_{1/2}$ = −0.55 V).[13] When $\Delta E_{1/2}$ lies between −0.2 and −0.3 V the 1,4-dihydro derivatives can be isolated under nitrogen, e.g., 5,12-dihydrophenazine ($E_{1/2}$ = −0.36 V),[32] and when $\Delta E_{1/2}$ is less negative than −0.2 V, the compounds can be isolated without any special care as in the case of **3c** ($E_{1/2}$ = −0.21 V) and **4c** ($E_{1/2}$ = −0.25 V). These last two products are only slowly oxidized in solution. As in the case of pyridopyrazines, it appears that the different positions of the nitrogen in the pyridine ring do not influence the reduction mechanism.

Aprotic Medium. Behavior of 1. In acetonitrile (c = 10^{-3} M) the cyclic voltammogram (v = 0.2 V s^{-1}) of 1 shows two reversible peaks at Ep_{C_1} = −0.98 V and Ep_{C_2} = −1.65 V. As in the case of pyridopyrazines[13] and aromatic hydrocarbons,[33] this voltammogram corresponds to the reduction scheme shown in Scheme I.

Upon addition of phenol the second couple progressively disappears while the first cathodic and anodic peaks increase in height up to bielectronic behavior while shifting to more positive potentials; for a 10^{-2} M concentration of phenol Ep_C = −0.83 V and Ep_A = −0.56 V. The electrolysis of a dilute solution (c = 10^{-3} M, c(phenol) = 0.1 M, E = −1.2 V) consumes 2 F/mol, and analysis of the resulting solution (UV, polarogram) shows that **3c** is obtained quantitatively.

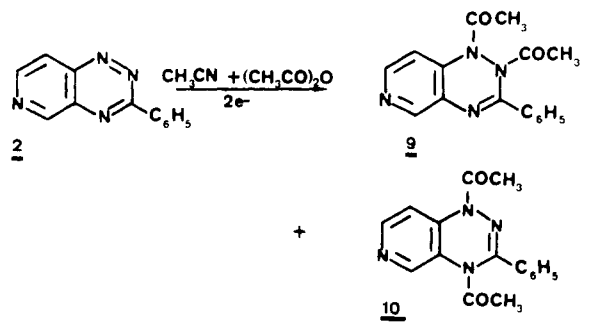


Scheme II



In the same way the second couple observed on the voltammogram progressively disappears on addition of acetic anhydride while the first cathodic and anodic waves increase in height up to 2e behavior for $c((CH_3CO)_2O)$ > 5×10^{-2} M while shifting to more positive potentials: for $c((CH_3CO)_2O)$ = 0.1 M, Ep_C = −0.71 V and Ep_A = −0.36 V. An attempted preparative electrolysis yielded only gummy products.

Behavior of 2. In acetonitrile alone or in the presence of phenol, 2 shows the same behavior as 1. In acetonitrile the two reversible couples on the voltammogram are observed at Ep_{C_1} = −0.88 V and Ep_{C_2} = −1.60 V. The addition of acetic anhydride, as in the case of 1, shifts the first couple to more positive potentials and increases its height while the second couple disappears. But in the case of **2**, a preparative electrolysis leads to a 75:25 mixture of the diacetyl derivatives **9** and **10**. A pure sample of **9** was



obtained upon recrystallization from methanol. The diacetyl derivative **10** was prepared by heating **4c** in the presence of acetic anhydride. The NMR spectrum of the raw product shows that, after 2 h of heating, a 57:43 mixture of **9** and **10** is obtained and that the relative amount of **10** increases with the time: 41:59 after 7 h and 26:74 after 14 h.

The room temperature NMR spectra of **9** and **10** shows the existence of two *N,N'*-diacetyl groups but do not indicate their positions. The assignment of the structures was based on conformer analysis at low temperature.[34]

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(33) R. Dietz in "Organic Electrochemistry", M. M. Baizer, Ed., marcel Dekker, New York, 1973, p 253.
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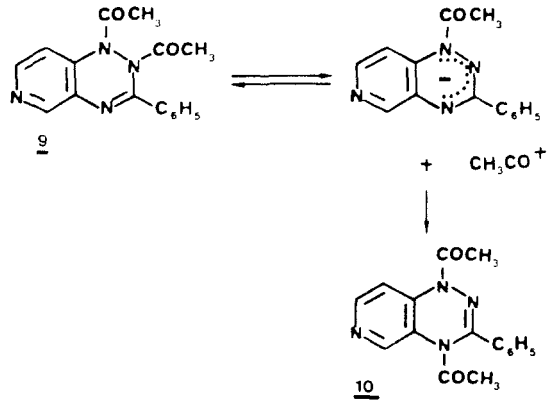
Scheme III



The formation of **10** by electrochemical reduction resembles the formation of 1,4-dihydro-1,4-diacetylquinoxaline under similar conditions.[35] The ecec scheme shown in Scheme II rationalizes the simultaneous formation of **9** and **10**.

Since **9** isomerizes to **10** on being heated, the latter compound must be thermodynamically more stable, and the formation of **9** during electrolysis must be kinetically controlled. This isomerization of **9** to **10** is similar to that of 2-acetylindazole to 1-acetylindazole,[36] and the reaction scheme shown in Scheme III can account for the results.

In acetonitrile in the presence of phenol or acetic anhydride, only the triazine ring is reduced, while with pyridopyrazines the reduction involves one ring or the other.[13]

Experimental Section

Melting points are uncorrected. UV spectra were recorded on a Beckmann 25 spectrometer and mass spectra on a JEOL JMS B-100 (75 eV, 300 mA) spectrometer.

^1H and ^{13}C NMR spectra were obtained on Bruker WH 90, Varian EM 360, and Varian XL-100-12 WG spectrometers with tetramethylsilane as an internal standard in $CDCl_3$ and hexamethyldisiloxane (HMDS) in CD_3SOCD_3 as a standard in Me_2SO-d_6.

For NOE experiments the samples were carefully degassed by three freeze–pump–thaw cycles. The apparatus and techniques used for the electrochemical studies and pH measurements have been described previously;[13] all the potentials are referred to the saturated calomel electrode; the temperature of the solutions was 20 °C. The microanalyses were performed by the microanalyses department of INSCIR.

Preparation of Pyrido-*as*-triazines. Compounds **1**, **2**, and **6** were prepared as described in the literature.[21-23] The other 3-arylpyrido[3,4-*e*]-*as*-triazines were synthesized according to the procedure used for **2** and purified by sublimation.

3-(2′-Furyl)pyrido[3,4-*e*]-*as*-triazine: mp 144 °C; ^1H NMR (Me_2SO-d_6) δ (HMDS) 6.8 (dd, 1 H, J = 3.5, 2 Hz, $H_{4'}$), 7.73 (dd, 1 H, J = 3.5, 2 Hz, $H_{5'}$), 8.08 (m, 1 H, J = 2, 1 Hz, $H_{3'}$), 8.33 (dd, 1 H, J = 6, 1 Hz, H_8), 8.86 (d, 1 H, J = 6 Hz, H_7), 9.55 (d, 1 H, J = 1 Hz, H_5). Anal. Calcd for $C_{10}H_6N_4O$: C, 60.61; H, 3.05; N, 28.27. Found: C, 60.53; H, 3.15; N, 28.41.

3-(2′-Thienyl)pyrido[3,4-*e*]-*as*-triazine: mp 148 °C; ^1H NMR (Me_2SO-d_6) δ (HMDS) 7.25 (dd, 1 H, J = 5.5, 4 Hz, $H_{4'}$), 7.90 (dd, 1 H, J = 5.5, 1.5 Hz, $H_{5'}$), 8.20 (dd, 1 H, J = 4, 1.5 Hz, $H_{3'}$), 8.30 (dd, 1 H, J = 5.5, 1 Hz, H_8), 8.83 (d, 1 H, J = 5.5 Hz, H_7), 9.48 (d, 1 H, J = 1 Hz, H_5). Anal. Calcd for $C_{10}H_6N_4S$: C, 56.08; H, 2.82; N, 26.16. Found: C, 55.84; H, 2.97; N, 26.23.

3-(2′-Pyrrolyl)pyrido[3,4-*e*]-*as*-triazine: mp 197 °C; ^1H NMR (Me_2SO-d_6) δ (HMDS) 6.25 (m, 1 H, $H_{4'}$), 7.15 (m, 1 H, $H_{3'}$), 7.30 (m, 1 H, $H_{5'}$), 8.25 (dd, 1 H, J = 5.5, 1 Hz, H_8), 8.75 (d, 1 H, J = 5.5 Hz, H_7), 9.37 (d, 1 H, J = 1 Hz, H_5), 12.2 (br s, 1 H, $H_{1'}$). Anal. Calcd for $C_{10}H_7N_5$: C, 60.91; H, 3.58; N, 35.51. Found: C, 61.26; H, 3.27; N, 35.60.

3-(2′-Indolyl)pyrido[3,4-*e*]-*as*-triazine: mp 265 °C; ^1H NMR (Me_2SO-d_6) δ (HMDS) 7.08 (m, 4 H, H_4, H_5, H_6, H_7), 7.91 (s, 1 H, $H_{3'}$), 8.57 (dd, 1 H, J = 5.5, 1 Hz, H_8), 9.06 (d, 1 H, J = 5.5 Hz), 9.75 (d, 1 H, J = 1 Hz, H_5). Anal. Calcd for $C_{14}H_9N_5$: C, 68.01; H, 3.67; N, 28.32. Found: C, 68.25; H, 3.66; N, 27.93.

p*K* Measurements. The pK values of **3c** and **4c** were determined spectrophotometrically. The solutions (50% aqueous CH_3OH, c = 10^{-3} M) were deoxygenated with argon. NaCl was used to maintain a constant ionic strength (μ = 0.2 M). The buffers were H_2SO_4, H_3PO_4–Na_2HPO_4, CH_3COOH–CH_3COONa, NaH_2PO_4–Na_2HPO_4, and $NaHCO_3$–Na_2CO_3. The temperature was maintained at 20 °C. The following UV data were obtained: **3c** (spectrum at pH 7), λ_{max} 345 nm (ε 5600); (**3c**)H^+ (spectrum at pH 1.5), 375 nm (ε 4600), 425 (4300, sh) (pK = 4.42 ± 0.05); **4c** (spectrum at pH 10), λ_{max} 320 nm (ε 2650), 385 (1000, sh); (**4c**)H^+ (spectrum at pH 3), 335 nm (ε 4050), 470 (1750) (pK = 7.28 ± 0.05).

Hydrogenation of 1 and 2: Preparation of 3c and 4c. Catalytic hydrogenation was carried out at room temperature with 500 mg of **1** in 150 mL of methanol in the presence of 150 mg of 10% Pd/C. After 2 h of stirring and consumption of 1 mol of H_2/mol of **1** the solution was filtered and evaporated to dryness to give a solid (**3c**) which was washed with petroleum ether: 450 mg (90%); mp 135 °C; mass spectrum, m/e 210 (M^+). Anal. Calcd for $C_{12}H_{10}N_4$: C, 68.56; H, 4.79; N, 26.65. Found: C, 68.40; H, 4.90; N, 26.50.

With the same procedure 500 mg of **2** gave 460 mg (92%) of **4c**: mp 122 °C; mass spectrum, m/e 210 (M^+). Anal. Calcd for $C_{12}H_{10}N_4$: C 68.56; H, 4.79; N, 26.65. Found: C, 68.45; H, 4.86; N, 26.50.

Reduction of 1, 2, and 6 with $LiAlH_4$. Preparation of 5, 7, and 8. To a solution of **1** (700 mg) in THF (150 mL) was added $LiAlH_4$ (500 mg) portionwise in 1 h at 0–5 °C. The temperature was then raised to 20 °C. After being allowed to stand 2 h, the mixture was quenched with 50 mL of 5% aqueous KOH solution and then extracted with $CHCl_3$. The extracts were dried over Na_2SO_4 and evaporated. The residue was chromatographed on alumina (chloroform–methanol, 19:1, as eluant) to give 250 mg (35%) of **5**: mp 155 °C; mass spectrum, m/e 212 (M^+); ^1H NMR (Me_2SO-d_6) δ (HMDS) 1.88 (m, 2 H, J = 6 Hz, H_6), 2.80 (t, 2 H, J = 6 Hz, H_5), 3.3 (t, 2 H, H_7), 7.3 (m, 3 H, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.66 (br s, 1 H, H_8), 8.1 (m, 2 H, $H_{2'}$, $H_{6'}$). Anal. Calcd for $C_{12}H_{12}N_4$: C, 67.91; H, 5.70; N, 26.40. Found: C, 67.59; H, 5.95; N, 26.10.

With the same work up, 1 g of **6** gave 0.1 g (10%) of **7**: mp 86 °C; mass spectrum, m/e 136 (M^+); ^1H NMR ($CDCl_3$) δ (Me_4Si) 2.05 (quintet, 2 H, J = 6, 5 Hz, H_6), 2.90 (t, 2 H, J = 6 Hz, H_5), 3.50 (t, 2 H, J = 5 Hz, H_7), 6.6 (br s, 1 H, H_8), 8.75 (s, 1 H, H_3). Anal. Calcd for $C_6H_8N_4$: C, 52.93; H, 5.92; N, 41.15. Found: C, 53.10; H, 6.15; H, 40.90.

With the same procedure, 1 g of **2** was reduced with 0.8 g of $LiAlH_4$ and gave 0.5 g (50%) of **8**: mp 215 °C; mass spectrum, m/e 212 (M^+); ^{13}C NMR (Me_2SO-d_6) δ 151.5 (s, C_3), 144 (s, C_9), 132.5 (d, C_7, $^1J_{C_7-H_7}$ = 170 Hz), 130.4 (d, $C_{4'}$, $^1J_{C_{4'}-H_{4'}}$ = 160 Hz), 129.2 (s, $C_{1'}$), 128.5 (d, $C_{3'}$, $^1J_{C_{3'}-H_{3'}}$ = 160 Hz), 126.8 (d, $C_{2'}$, $^1J_{C_{2'}-H_{2'}}$ = 160 Hz), 91.5 (d, C_8, $^1J_{C_8-H_8}$ = 165 Hz), 48.8 (d, C_{10}, $^1J_{C_{10}-H_{10}}$ = 140 Hz), 46.4 (t, C_5, $^1J_{C_5-H_5}$ = 140 Hz). Anal. Calcd for $C_{12}H_{12}N_4$: C, 67.91; H, 5.70; N, 26.40. Found: C, 67.72; H, 5.78; N, 26.30.

Electrolysis of 2 in CH_3CN in the Presence of Acetic Anhydride. Preparation of 9. Electrolysis was carried out according to the technique described previously[13] at E = −1.4 V (SCE). The cathodic solution contained 60 mL of CH_3CN, 8 mL of acetic anhydride, 2.2 g of tetrabutylammonium iodide, and 1 g of **2**. During electrolysis a polymeric product precipitated. At the end of electrolysis (2 F/mol) the solution was filtered and the filtrate poured into 500 mL of water. The mixture was neutralized with $NaHCO_3$ and extracted with ether. The extracts were dried over Na_2SO_4 and evaporated. The residue was essentially (NMR spectrum) a mixture of **9** and **10** (75:25). Recrystallization from methanol gave 310 mg (22%) of **9**: mp 146 °C; mass spectrum, m/e 294 (M^+); ^1H NMR ($CDCl_3$) δ (Me_4Si) 2.00 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 7.2–9 (m, 8 H, C_6H_5, H_7, H_8, H_9). Anal. Calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.46; H, 4.90; N, 18.91.

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Acetylation of 4c. Preparation of 10. Compound 4c (1 g) was heated under reflux for 12 h with acetic anhydride (20 mL). The excess acetic anhydride was evaporated and the residue poured into ethanol–water (50:50). The precipitate was filtered and recrystallized from ethanol/water (50:50) to give 1 g (71%) of 10: mp 148 °C; mass spectrum, *m/e* 294 (M^+); ^1H NMR spectrum ($CDCl_3$) δ (Me_4Si) 2.03 (s, 3 H, CH_3), 2.58 (s, 3 H, CH_3), 7.3–9 (m, 8 H, C_6H_5, H_5, H_7, H_8). Anal. Calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.20; H, 4.96; N, 18.90.

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Registry No. 1, 59850-36-1; 2, 40848-48-4; 3c, 60097-00-9; 4c, 60445-75-2; 5, 78149-61-8; 6, 6133-44-4; 7, 78149-62-9; 8, 78149-63-0; 9, 78149-64-1; 10, 78149-65-2; 3-(2′-furyl)pyrido[3,4-*e*]-*as*-triazine, 78149-66-3; 3-(2′-thienyl)pyrido[3,4-*e*]-*as*-triazine, 78149-67-4; 3-(2′-pyrrolyl)pyrido[3,4-*e*]-*as*-triazine, 78149-68-5; 3-(2′-indolyl)-pyrido[3,4-*e*]-*as*-triazine, 78149-69-6.

Chemistry of 1,5-Diazapentadienium (Vinamidinium) Salts: Alkylation Reactions to Multifunctional Dienamines and Dienaminones[1]

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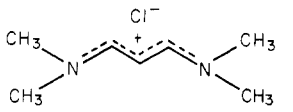
1,5-Diazapentadienium chloride 1 is a push–pull 6-π-electron system. It reacts selectively and in high yields with enolates of cyclic and acyclic ketones, esters, lactones, and lactams to produce multifunctional dienaminones. Heterocyclic systems containing activated methylene groups such as 2-ethyl-2-oxazoline, 2-picoline, and 2-methylfuran are converted to reactive dienamines. Derivatives of γ,δ-unsaturated β-keto esters, useful intermediates in organic synthesis, can be synthesized directly by selective alkylation with 1 of the dianion derived from ethyl acetoacetate. Cyclopentane-1,3-dione methyl ether reacts with 1 to produce both *E,E* and *Z,E* alkylated products.

One of the major synthetic applications of compounds containing activated methylene groups is the selective alkylation of the carbon α to the carbonyl group.[2,3] The enols and enolates of these carbonyl compounds have been alkylated with a variety of alkyl and allyl halides, as well as alkyl sulfonates, tosylates, oxonium ions and other reagents. We report the use of vinamidinium salts[4] in the alkylation of carbonyl enolates to produce dienaminones. The reaction appears to have generality, and we have applied it successfully to diesters, keto esters, cyclic and acyclic ketones, lactones, lactams, and other compounds containing activated methylene groups. The dienaminones and dienamines formed in these reactions are multifunctional compounds that have potential as intermediates in the synthesis of some natural products.

The vinamidine system (1,5-diaza-1,3-pentadiene) is present in natural products such as the betacyanin pigments found in red beets, many cacti, pokeberry and other plants[5] and in the porphyrin and corrin ring systems of chlorophyll, hemoglobin, cytochromes, and vitamin B_{12}.[6] Vinamidinium salts such as 1 are examples of push–pull alkenes, compounds that are stabilized by groups which can donate or accept electrons. They are vinylogues of amidinium salts and have an alternation of electron density; the α-carbons are electron poor and are attacked by nucleophilic reagents, and the β-carbon is electron rich and is attacked by electrophilic reagents.[7,8] The enhanced stability and push–pull nature of the vinamidinium system gives it regenerative character which makes it prone to substitution rather than addition reactions. The regenerative character of the vinamidinium salts has been demonstrated in both electrophilic reactions such as halogenation, nitration, and Vilsmeier type alkylations,[9] and in nucleophilic reactions with amines and carbon nucleophiles. The nucleophilic reactions have been exploited the most and have led to the synthesis of some polycyclic aromatic and heterocyclic compounds.[10–12] Vinamidinium salts have been used to alkylate the activated methylenes of various nitriles,[12,13] but there is only one report of the alkylation of other types of activated methylene compounds.[14]

Results and Discussion

In previous work with vinamidines, the perchlorate salts were used.[15] In this work we found a convenient method for the preparation of the tetramethylvinamidinium chloride salt 1 in good yield using readily available com-



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mercial reagents. This procedure involved the preparation of β-(dimethylamino)acrolein by a Vilsmeier reaction on

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