t-3,t-5-Dimethyl-N-nitroso-r-2,c-6-diphenylpiperidin-4-one (14). Nitrosation of **5** (0.80 g, 2.86 mmol) was performed by the same procedure as used for **11**. **14**: yield 0.65 g (73.8%); colorless spongy solid; mp 164–166 °C, lit.[20e] mp 166–167 °C; IR (KBr) 1720, 1440, 1180, 1160, and 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, J = 6.6 Hz, 3 H), 1.22 (d, J = 7.3 Hz, 3 H), 3.03 (m, 1 H), 3.52 (m, 1 H), 5.22 (d, J = 10.01 Hz, 1 H), 6.16 (d, J = 3.0 Hz, 1 H), and 6.7–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 12.4, 15.7, 44.5, 45.4, 61.7, 65.9, 127.5, 127.7, 128.4, 128.7, 129.1, 137.3, 138.2, and 209.5; MS m/z 308, 291, 264, 263, 207, 194, 190, 160, 134, 132, 118, 117, 104, 91, 89, 77, 65, and 57. Anal. ($C_{19}H_{20}N_2O_2$) C, H, N.

N-Nitroso-r-2,t-3,t-5,c-6-tetraphenylpiperidin-4-one (15). A mixture of **6** (1.1 g, 2.72 mmol) and concentrated HCl (0.4 mL dissolved in a 1:1 ethanol–water mixture (75 mL)) was prepared. The nitrosation was carried out by the addition of a $NaNO_2$ solution (0.21 g in 15 mL of a 1:1 ethanol–water mixture) as in the previous cases. The crude product was crystallized twice from ethanol. **15**: yield 0.85 g (72.3%); colorless crystals; mp 169–171 °C; IR (KBr) 1715, 1330, 1180, 1170, and 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.41 (d, J = 7.7 Hz, 1 H), 4.54 (d, J = 6.4 Hz, 1 H), 6.15 (d, J = 7.7 Hz, 1 H), 6.32 (d, J = 6.4 Hz, 1 H), and 6.8–7.3 (m, 20 H); ^{13}C NMR ($CDCl_3$) δ 57.6, 58.0, 59.2, 66.0, 126.7, 127.8, 128.0, 128.3, 128.5, 128.6, 128.7, 129.0, 133.3, 135.5, 137.0, 138.0, and 205.4; MS m/z 432, 402, 222, 194, 179, 165, 152, 107, 105, 97, 91, and 77. Anal. ($C_{29}H_{24}N_2O_2$) C, H, N.

N-Nitroso-r-2,c-6-diphenylpiperidine (16). Nitrosation of **7** by the above procedure (0.70 g, 2.95 mmol) yielded **16**. The product was recrystallized twice from ethanol. **16**: yield: 0.45 g (57.3%); pale yellow crystals; mp 68–69 °C, lit.[20d] mp 66.5–67.5 °C; IR (KBr) 1490, 1430, 1350, 1190, 1160, and 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72–1.92 (m, 2 H), 2.03–2.30 (m, 3 H), 2.50–2.62 (m, 1 H), 6.00–6.07 (m, 2 H), 6.75–7.25 (m, 10 H); ^{13}C NMR ($CDCl_3$) 17.3, 26.9, 27.0, 51.9, 60.4, 126.7, 126.8, 127.3, 127.4, 127.9, 128.1, 138.4, and 139.1; MS m/z 266, 249, 236, 221, 194, 165, 145, 131, 117, 104, 91, 77, 65, and 51. Anal. ($C_{17}H_{18}N_2O$) C, H, N.

t-3-Methyl-N-nitroso-r-2,c-6-diphenylpiperidine (17). The crude product obtained by nitrosating **8** (0.75 g, 2.98 mmol) was crystallized twice from ethanol. **17**: yield 0.38 g (45.5%); pale yellow crystals; mp 62–64 °C; IR (KBr) 1490, 1440, 1340, 1190, and 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, J = 8.1 Hz, 1.35 H), 1.12 (d, J = 8.4 Hz, 1.65 H), 1.4–1.6 (m, 1 H), 2.1–2.8 (m, 4 H), 5.28 (d, J = 7.8 Hz, 0.45 H), 5.57 (d, J = 5.4 Hz, 0.55 H), 5.78 (t, J = 6.6 Hz, 0.55 H), 6.14 (dd, J = 4.0 and 7.2 Hz, 0.45 H), 6.8–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 19.1, 20.5, 24.2, 25.7, 25.9, 26.2, 31.4, 31.9, 54.2, 60.3, 62.0, 68.1, 126.4, 126.7, 126.8, 127.4, 127.6, 127.7, 127.8, 128.0, 128.1, 128.4, 138.4, 139.1, 139.6, and 140.1; MS m/z 280, 263, 250, 235, 194, 156, 145, 131, 117, 104, 91, 77, 65, and 51. Anal. ($C_{18}H_{20}N_2O$) C, H, N.

t-3,c-5-Dimethyl-N-nitroso-r-2,c-6-diphenylpiperidine (18). Nitrosation of **9** (0.75 g, 2.83 mmol) was carried out by the same procedure as described above. The crude product was crystallized twice from ethanol. **18**: yield 0.54 g (62.5%); pale yellow crystals; mp 76–77 °C; IR (KBr) 1460, 1420, 1380, 1350, 1230, 1180, 1170, and 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (d, J = 6.6 Hz, 1 H), 0.98 (d, J = 6.9 Hz, 0.5 H), 1.08 (d, J = 6.6 Hz, 1 H), 1.14 (d, J = 6.6 Hz, 0.5 H), six multiplets at 1.54, 1.7, 2.06, 2.4, 2.7, and 2.92 account for 4 protons, 5.27 (d, J = 7.6 Hz, 0.6 H), 5.52 (d, J = 5.9 Hz, 0.4 H), 5.79 (d, J = 6.1 Hz, 0.6 H), 6.02 (d, J = 6.1 Hz, 0.4 H), and 6.6–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 18.1, 18.7, 18.8, 19.7, 28.3, 29.9, 30.2, 31.8, 33.2, 33.6, 55.4, 58.7, 66.6, 66.8, 126.7, 127.1, 127.2, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.6, 128.8, 128.9, 129.6, 136.2, and 139.0; MS m/z 294, 277, 264, 194, 172, 159, 145, 131, 117, 105, 91, 77, 65, and 51. Anal. ($C_{19}H_{22}N_2O$) C, H, N.

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Electrochemical and Chemical Reduction of Furopyrazines, Thienopyrazines, Furoquinoxalines, and Thienoquinoxalines

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The electrochemical reduction of furopyrazines, thienopyrazines, furoquinoxalines, and thienoquinoxalines was investigated in protic and aprotic mediums. The thieno[2,3-*b*]pyrazines and the thieno[3,4-*b*]pyrazines both lead, in aqueous medium, to a dihydro compound where the two nitrogen atoms of the pyrazine ring are hydrogenated. These primary reduction products isomerize in different ways: in the [2,3-*b*] series the thiophene ring is reduced while in the [3,4-*b*] series the pyrazine ring is reduced. These results can be rationalized on the basis of quantum calculations of the energies of the different isomers. These calculations also permit the explanation of the different reducibility between the two series of compounds.

The electrochemical reduction in protic medium of heterocyclic compounds containing a pyrazine ring has been shown[1-9] to lead to 1,4-dihydro derivatives. Some dihydro compounds, where the two pyrazine nitrogen are hydrogenated, are stable. This is, for example, the case with 7,8-dimethylpyrido[2,3-*b*]quinoxaline[9] (**1**) and with

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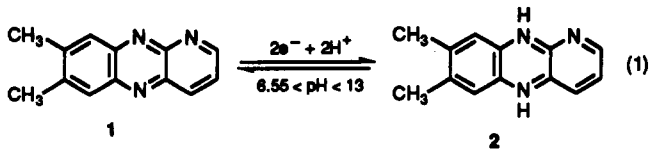
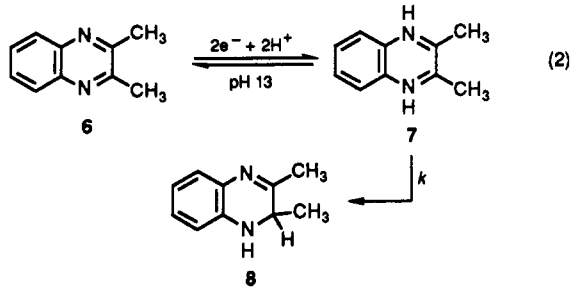
pyrazino[2,3-*b*]phenazine.[8] Thus, 2,3-bis(*p*-methoxy-



(1)

1 2

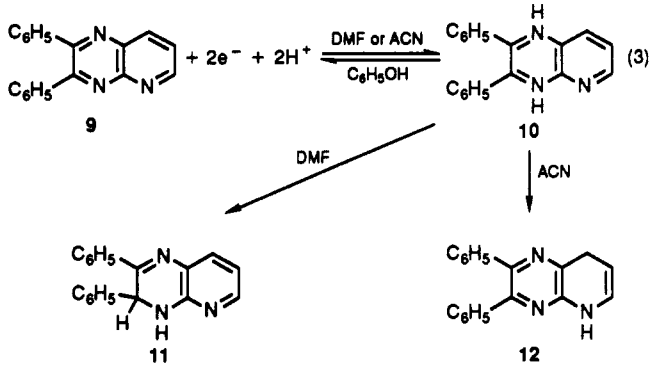
phenyl)pyrazino[2,3-*b*]phenazine (3) is reduced at pH 8 to a 6,11-dihydro compound 4 and then to a 1,4,6,11-tetrahydro derivative 5. But most often these dihydro compounds 7 rearrange to another dihydro derivative 8, as with quinoxalines.[1] When different rearranged prod-



(2)

6 7 8

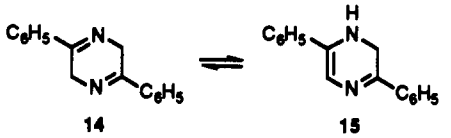
ucts can be obtained, shifting the course of the reaction from one isomer to the other can be accomplished by very small changes in the experimental conditions. For example,[5] by changing from acetonitrile (ACN) to dimethylformamide (DMF) one can obtain compound 11 where the pyrazine ring is reduced, instead of a compound 12 where the pyridine ring is reduced:



(3)

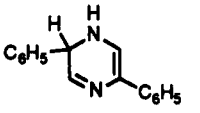
9 10 11 12

It is not generally possible to observe the interconversion of the transposed isomers such as 11 ↔ 12. But in the case of 2,5-diphenylpyrazine 13 it is possible[4] to observe (in $CDCl_3$ at room temperature) a thermodynamic equilibrium between the 2,5-diphenyl-3,6-dihydropyrazine (14) and the 2,5-diphenyl-1,6-dihydropyrazine (15):



14 15

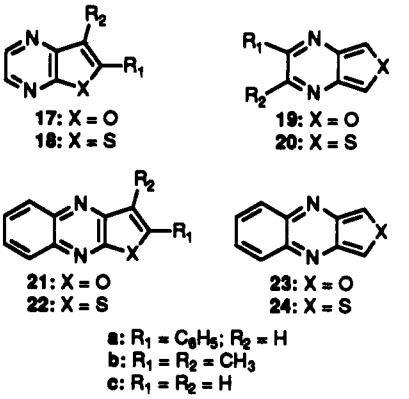
In this case, it must be noted that the 2,5-diphenyl-1,2-dihydropyrazine (16) is never observed; indeed, it should be less stable as only one phenyl group is conjugated to the dienic system in a cross-conjugated way.



16

With all the previous compounds the rearrangement of the initially formed 1,4-dihydropyrazine derivatives thus seems under control of an interplay of thermodynamic and kinetic parameters.

In this paper, we shall attempt to rationalize these transpositions with the help of quantum calculations of the energies of the different isomers obtained. These calculations will also permit an interpretation of the difference of reduction potentials with the structure of the compounds. The compounds investigated for this purpose were furo[2,3-*b*]pyrazines 17, thieno[2,3-*b*]pyrazines 18, thieno[3,4-*b*]pyrazines 20, furo[2,3-*b*]quinoxalines 21, and thieno[2,3-*b*]quinoxalines 22.



Furo[3,4-*b*]pyrazines 19 and furo[3,4-*b*]quinoxaline (23) have not been synthetized until now, and the thieno[3,4-*b*]quinoxaline (24) is too unstable to be investigated by electrochemistry; its transient existence could only be observed by trapping experiments.[10] The synthesis of **17a**, **18a**, **20a**, **20b**, **21a**, and **22a** is described in the Experimental Section.

Table I. Polarographic Two-Electron Half-Wave Potentials in H_2O/MeOH = 50/50

17a	$1 \le pH \le 5$	$E_{1/2}$[a] = −0.38−0.083pH
		$E_{1/2}$ = −0.54−0.056pH
18a	$1 \le pH \le 4.8$	$E_{1/2}$ = −0.36−0.079pH
	$4.8 \le pH \le 13$	$E_{1/2}$ = −0.46−0.057pH
20a	$1 \le pH \le 13$	$E_{1/2}$ = −0.22−0.085pH
21a	$1 \le pH \le 13$	$E_{1/2}$ = −0.29−0.059pH
22a	$1 \le pH \le 13$	$E_{1/2}$ = −0.12−0.059pH

[a] In V/SCE.

Results

Furo[2,3-*b*]pyrazines 17 and Thieno[2,3-*b*]-pyrazines 18. The electrochemical behavior of **17a** and **18a** (R_1 = C_6H_5, R_2 = H) in aprotic medium (dry ACN) is similar to that of quinoxalines: by cyclic voltammetry, a first reversible system is accompanied by an irreversible peak. The reversible peak leads to the formation of a stable radical anion $17^{\bullet-}$ and $18^{\bullet-}$ but the very basic diamines obtained after the second peak are protonated by

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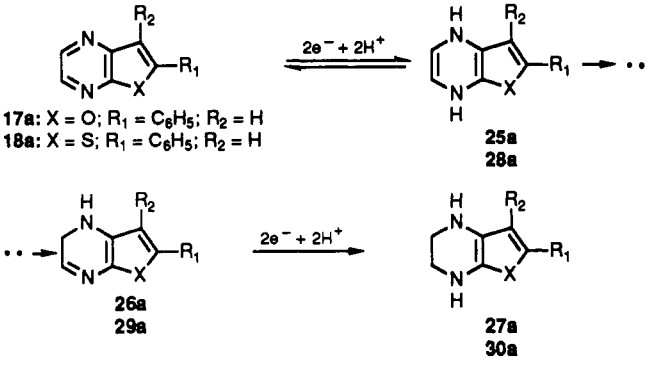
Table II. Redox ($E°$) and Peak (E_p) Potentials[a,b] in Aprotic Medium[c]

	$E°_1$ reversible	E_{pc2} irreversible
quinoxaline	−1.62	−2.63
phenazine	−1.19	−1.84
17a	−1.70	−2.28
18a	−1.65	−2.12
20a	−1.44	−1.90
20b	−1.65	−2.09
21a	−1.44	−2.15
22a	−1.38	−1.97

[a] In V/SCE. [b] Peak potentials at 0.2 V s^{-1}. [c] In dry ACN + 0.1 M NBu_4BF_4.

Scheme I



the solvent and any residual water. The peak potentials are given in Table I.

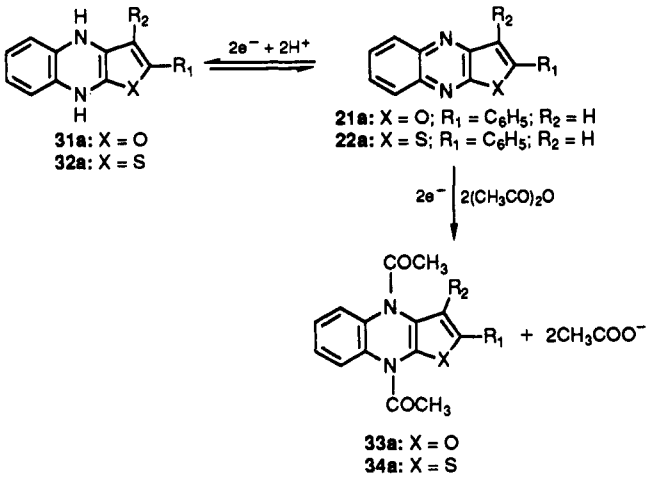
In protic medium (H_2O/MeOH = 50/50) the polarogram of **17a** shows a pH-dependent two-electron wave (Table II). A controlled potential electrolysis at pH 13 leads to 4,5(or 6,7)-dihydro-2-phenylfuro[2,3-*b*]pyrazine (**26a**). It displays a two-electron cathodic wave at pH 13 ($E_{1/2}$ = −1.62 V) that is not observed on the polarogram of **17a**, indicating that **26a** is not the primary reduction product of **17a**. The cyclic voltammogram of **17a** at 0.2 V s^{-1} shows a reversible system (H_2O/MeOH = 50/50, pH 13) at $E°$ = −1.16 V/SCE. The behavior of **17a** is thus similar to that of other pyrazine derivatives, and the reversible system observed by cyclic voltammetry is that of **17a** ↔ **25a** where **25a** is the primary reduction product that rearranges to **26a** (Scheme I).

A similar behavior is observed for the thieno[2,3-*b*]-pyrazine **18a**; a two-electron polarographic wave is observed (Table II). It appears that **18a** is slightly easier to reduce than **17a** ($\Delta E_{1/2}$ = 0.07 V at pH 7). The electrolysis of **18a** at pH 13 gives **29a**, while a cyclic voltammogram at pH 13 affords a two-electron reversible system at 0.2 V s^{-1}, $E°$ = −1.19 V/SCE. **29a** displays a two-electron cathodic wave at pH 13, and a controlled potential electrolysis gives **30a**.

Thus, both the furo and the thieno derivatives fit into the general reduction pattern of pyrazine derivatives where the primary reduction product is the dihydro derivative where the pyrazine ring is reduced on both nitrogens. This primary reduction product rearranges to another dihydro derivative (**26a** and **29a**). In the case of furo- and thieno[2,3-*b*]pyrazines, the aromaticity of the pyrazine ring is lost while that of the furo or thieno cycles is maintained.

The chemical reduction of **17a** and **18a** has also been investigated: no reaction was observed with $NaBH_4$, $LiAlH_4$, CH_3MgCl, or catalytic hydrogenation (p_{H_2} = 60 bar). This result is in sharp contrast with the behavior of quinoxalines, which are easily reduced by $NaBH_4$ and $LiAlH_4$, are easily hydrogenated at room pressure, and easily add 2 mol of organomagnesium derivatives.

Scheme II



Furo[2,3-*b*]quinoxalines 21 and Thieno[2,3-*b*]-quinoxalines 22. The electrochemical reduction of **21a** and **22a** (R_1 = C_6H_5, R_2 = H) in aprotic medium (dry ACN) leads to a first reversible and a second irreversible peak as in the case of phenazine. The peak potentials are given in Table I.

In protic medium (H_2O/DMF = 50/50), **21a** shows a pH-dependent two-electron wave (Table II). A controlled potential electrolysis at pH 7 (E = −1.0 V) of a millimolar solution allows us to observe an anodic wave, the $E_{1/2}$ of which is near that of the cathodic wave of **21a**. This wave corresponds to the reduction product **31a**, which cannot be isolated as it is highly oxidizable ($E_{1/2}$ = −0.69 V at pH 7 for **31a**). A similar behavior is observed for **22a** (Table II), and an electrolysis at pH 7 (E = −1.0 V) leads to **32a**, which is also too oxidizable to be recovered. In order to be able to isolate a stable compound, an electrolysis was performed in DMF in the presence of acetic anhydride to give good yields of **33a** and **34a**. These results are summarized in Scheme II. They are analogous to what is observed with phenazine; the reduced pyrazine ring does not isomerize.

Thieno[3,4-*b*]pyrazines 20. The cyclic voltammetry of **20a** (R_1 = C_6H_5, R_2 = H) and **20b** (R_1 = R_2 = CH_3) in dry ACN shows a reversible system and a second one-electron irreversible cathodic peak at the potentials shown in Table I.

It should be remarked that **20a** is more easily reduced than **18a** by $\Delta E°$ = 0.21 V.

In protic medium (H_2O/MeOH = 50/50), a two-electron wave is observed (Table II). In this medium, **20a** is also more easily reduced than **18a**: ΔE = 0.20 V at pH 7. A controlled potential electrolysis leads to the dihydro derivative **36a**. But cyclic voltammetry shows at pH 6.9 (H_2O/MeOH = 50/50) that **36a** is not the primary reduction product: on the cathodic scan (v = 0.2 V s^{-1}) a two-electron cathodic peak is observed for **20a** (E_{pc} = −0.72 V/SCE) and a two-electron anodic peak (E_{pa} = −0.55 V/SCE) is observed on the reverse scan; **36a** does not show any anodic wave by polarography, only a two-electron cathodic wave at $E_{1/2}$ = −0.95 V/SCE. This behavior is similar to that of quinoxalines, and the results are summarized in Scheme III. In basic medium the isomerization from **35a** to **36a** is slower than at pH 7; the polarograms recorded at pH 13 permit the observation of the anodic wave of **35a**, while no anodic wave is seen at pH 7. **20b** also shows a two-electron cathodic wave (Table II) and an electrolysis gives **36b**. A cyclic voltammogram of **20b** at pH 6.9 shows a cathodic peak at E_{pc} = −0.93 V and an anodic peak (E_{pa} = −0.62 V) on the reverse scan that can

Scheme III

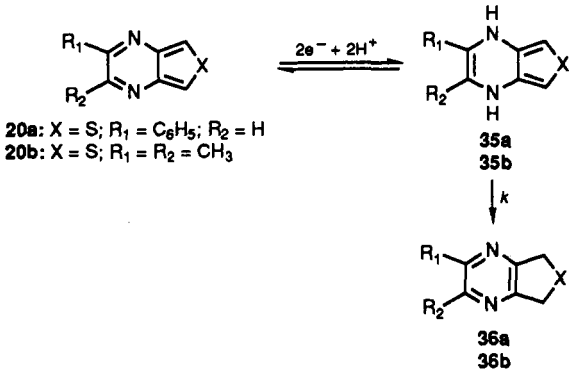


Table III. Calculated Energy (eV) for Anion Formation $\Delta\mathcal{E} = \mathcal{E}(Y^{\bullet-}) - \mathcal{E}(Y)$

Y	ΔE	Y	ΔE
17c	-1.08	19c	-1.23
17a	-1.35	19a	-1.35
18c	-1.26	20c	-1.59
18a	-1.45	20a	-1.69

be assigned to the oxidation of **35b**.

In contrast to the furo- and thieno[2,3-*b*]pyrazines, the thieno[3,4-*b*]pyrazine **20a** can be reduced by $NaBH_4$ and by catalytic hydrogenation, giving **36a**. CH_3MgCl reacts with **20a** to give 5,6-dihydro-5-methyl-4-phenylthieno-[3,4-*b*]pyrazine (**37a**).

Thiophene derivatives where the 2-position is unsubstituted are known to undergo electrochemical oxidation[11] leading to conductive polymers. In the case of **20a** and **20b**, an irreversible oxidation wave is observed in ACN at E_p = +1.78 V and E_p = +1.62 V, respectively, but no sign of polymerization could be observed; this is possibly due to the electron-withdrawing effect of the two nitrogens, but more likely the nucleophilicity of pyrazine is sufficient to quench the electrogenerated radical cation. It has been shown, for example, that amino groups prevent the polymerization of pyrrole.[12]

Discussion and Theoretical Analysis

The fact that in aprotic medium 4-phenylthieno[3,4-*b*]pyrazine (**20a**) is more easy to reduce (**20a** + e⁻ → **20a**$^{\bullet-}$) than 2-phenylthieno[2,3-*b*]pyrazine (**18a**; **18a** + e⁻ → **18a**$^{\bullet-}$) by 0.21 V appears as rather surprising. This difference cannot be accounted for by the presence of a 4-phenyl group in the case of **20a** as 2-phenylquinoxaline and quinoxaline have very similar redox potentials (E° = -1.59 and -1.62 V, respectively).

We therefore undertook structural and energy calculations in order to rationalize this difference of reducibility. MNDO calculations have been performed on the unsubstituted furo- and thienopyrazines **17c**, **18c**, **19c**, and **20c** and on the phenyl-substituted derivatives **17a**, **18a**, **19a**, and **20a**. Due to the size of studied systems (up to 15 heavy atoms), the semiempirical method MNDO was chosen. Though it is generally difficult to accurately describe anions, this method is convenient since (i) the charge is delocalized on a large system and (ii) we only discuss energy differences afforded by structural features on similar systems. In these conditions, these results must be regarded as semiquantitative landmarks showing general trends. Nevertheless, as can be seen in the following text, the agreement with experimental values, when available,

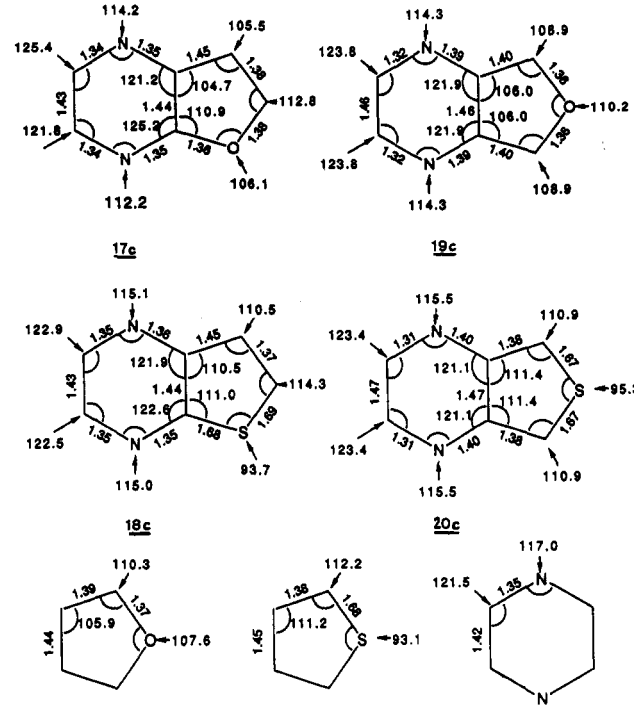


Figure 1. Calculated bond lengths and bond angles.

is good. Table III displays the relative energy of each radical anion with respect to the corresponding neutral species (the opposite of electron affinity). This value $\Delta\mathcal{E}$ reflects the reducibility of the molecule in aprotic medium, keeping in mind that solvation energies are not taken in account in these calculations. Thus, the difference $\Delta\mathcal{E}_{18a} - \Delta\mathcal{E}_{20a}$ = 0.24 V is close to the experimental value $E^\circ_{18a} - E^\circ_{20a}$ = 0.21 V (compare also $\Delta\mathcal{E}_{17a} - \Delta\mathcal{E}_{20a}$ = 0.34 V to $E^\circ_{17a} - E^\circ_{20a}$ = 0.26 V and $\Delta\mathcal{E}_{17a} - \Delta\mathcal{E}_{18a}$ = 0.10 V to $E^\circ_{17a} - E^\circ_{18a}$ = 0.05 V). Several points are worth some comments:

(1) The good agreement between the calculated and the available observed value indicate nearly equal changes in solvation passing from the molecule to the radical anion for all the molecules. As one can assume similar solvation energies for the neutral molecules, those of the radical anions must also be of similar magnitude. Besides, according to Marcus theory[13] changes in solvation energies are one of the factors that slow down electron transfers; as the voltammograms of **17a**, **18a**, and **20a** correspond to fast electron transfers under our experimental conditions, this implies small changes in solvation energies upon electron transfer.

(2) The examination of the form of LUMO of the neutral species, which is to accommodate the additional electron as well as the SOMO of the anion radical, shows the electron to be almost equally delocalized into each ring, in good agreement with a small change of solvation energy upon reduction.

(3) The derivatives **19** and **20** in the [3,4-*b*] series appear more reducible than the corresponding compounds **17** and **18** of the [2,3-*b*] series (Table III). Let us examine the unsubstituted series **17c**–**20c**. The variations in electron affinity are in qualitative agreement with the LUMO energy, which decreases according to **17c** (-0.770 eV), **19c** (-0.849 eV), **18c** (-0.929 eV), and **20c** (-1.235 eV). The better reducibility of this [3,4-*b*] series may appear to be in relation with geometrical contraints. For this purpose we report (Figure 1) the optimized geometries of furan,

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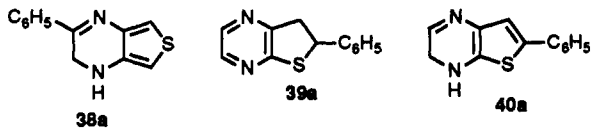
thiophene, and pyrazine as well as of **17c**, **18c**, **19c**, and **20c**. In the [3,4-*b*] series (**19c** and **20c**), the bond that is common to both cycles is obtained through the fusion of a carbon–carbon bond of the pyrazine ring with the rather long single bond of thiophene (1.45 Å) or furan (1.44 Å). On the other hand, in the [2,3-*b*] series (**17c** and **18c**), the fusion takes place with a shorter double bond (1.38 and 1.39 Å, respectively). The overall result is a better total overlap in the [2,3-*b*] series or, in other words, a more pronounced aromaticity. It agrees with the greater stability of **17c** ($R_1 = R_2 = H$) as compared to **19c** ($\Delta\mathcal{E}$ = 22.6 kJ mol^{-1}) and of **18c** as compared to **20c** ($\Delta\mathcal{E}$ = 45.9 kJ mol^{-1}). Moreover, one can remark, on the grounds of geometrical parameters, that the [3,4-*b*] compounds, resemble more an enimine system with alternant short and long bonds than an aromatic totally delocalized system. The decrease in the total overlap involves an increased HOMO energy (partly responsible for the destabilization of the neutral species) and a decreased LUMO energy leading to an increased reducibility.

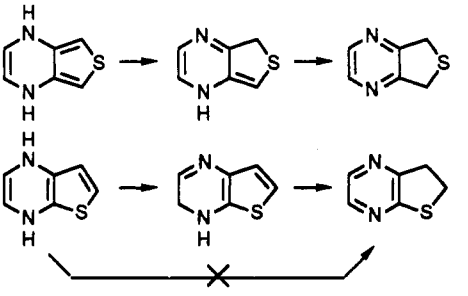
(4) As shown by calculations, the plane of the phenyl substituents is almost perpendicular to the bicyclic system (**17a**, 60°; **18a**, 73°; **19a**, 89°; **20a**, 80°), as observed for the 5,6-diphenylquinoxaline.[14] They only bring a weak perturbation, essentially due to their σ-acceptor character. This effect slightly stabilizes the MO's and thus increases the reducibility. The LUMO energy variation does not exceed 0.05 eV in this series. But, the [2,3-*b*] and [3,4-*b*] series are unequally affected. As a matter of fact, the LUMO exhibits a larger coefficient on the substituted center in the [2,3-*b*] series than in the [3,4-*b*] series: 0.44 for **17a** vs 0.35 for **19a** and 0.43 for **18a** vs 0.32 for **20a**. In the [2,3-*b*] series, the LUMO is more stabilized than in the [3,4-*b*] series, which tends to reduce the difference between the two series. In the case of the phenyl-substituted furo derivatives **17a** and **19a**, the same electron affinity is found for both compounds.

(5) The previous considerations also allow one to explain the low reactivity of **17a** and **18a** as compared to **20a** toward $NaBH_4$ and CH_3MgCl. There is evidence that both metal hydrides[15] and Grignard reagent[16] react as electron-transfer reagents.

Let us now consider the nature of the reduction products obtained by electrochemistry in protic medium. Our results show that **18a** as well as **20a** lead to the same type of dihydrogenated product **28a** and **35a**, which are analogous to the 1,4-dihydro derivatives obtained by reduction of pyrazines and quinoxalines. But in the present case, the puzzling point is that the reduced species **35a** isomerizes to **36a** where the aromaticity of the pyrazine is preserved, while **28a** rearranges to **29a** in which the aromaticity of thiophene is maintained, although the aromaticity of thiophene is weaker than that of pyrazine. The evolution of **35a** can be rationalized on thermodynamic grounds since the reaction **35a** → **36a** is found to be exothermic by 105.3 kJ mol^{-1} and the unobserved molecule **38a** is less stable than **36a** by 91.1 kJ mol^{-1}. Nevertheless,



although step **28a** → **29a** is still exothermic by 27.3 kJ mol^{-1} in the [2,3-*b*] series, the latter product is less stable than **39a**, which is not observed, by 47.2 kJ mol^{-1} (isomer **40a** is less stable than **29a** by only 2.7 kJ mol^{-1}, which is not significant, and does not allow one to specify the actual structure of the dihydro derivative). This suggests that the protons' transpositions are kinetically controlled, in agreement with the fact that no equilibrium can be observed even after several days under the electrolysis conditions. In both cases, the favored transpositions can be regarded as enamine–imine tautomery (double in the first case, single in the other), which are both easy, their rate being pH dependent; the imine form is highly favored. Indeed, in the cases of the heterocyclic compounds quoted in the introduction, the existence of even a small percentage of the enediamine form would lead to a fast and complete reoxidation of the samples. The double transposition, in the first case, allows the aromatization of the pyrazine moiety, more energetic than the thiophene, as expected and confirmed by the calculated energies. In the second case, the most stable system **39** cannot be reached through a sequence of enamine–imine 1,3-migration.



Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Bruker WH 80 and a Varian A 60 spectrometer using tetramethylsilane (TMS) as internal standard. The apparatus and techniques used for the electrochemical studies and pH measurements have been described previously.[5] All the potentials are referred to the saturated calomel electrode (SCE); the temperature of the solutions was 20 °C. Acetonitrile and dimethylformamide used in the cyclic voltammetric experiments were distilled and dried over activated alumina. The solutions were deoxygenated with nitrogen and dried over phosphorus pentoxide. The microanalyses were performed by the Service de Microanalyse, Université Pierre et Marie Curie. The following abbreviations are used in reporting NMR results: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet. All the compounds described gave correct elemental analysis.

Calculations have been performed using the MNDO 400 program. Parameters for C, H, N, O, and S are taken from refs 17 and 18, respectively. The geometrical parameters for the heterocycle moieties have been fully optimized, whereas the internal coordinates of phenyl substituents, when present, have been frozen with standard values. Nevertheless, the Ph–C bond length and the twisting angle of the phenyl have been optimized.

Preparation of Furopyrazines, Thienopyrazines, Furoquinoxalines, and Thienoquinoxalines. 2-Phenylfuro[2,3-*b*]pyrazine (**17a**) and 2-phenylthieno[2,3-*b*]pyrazine (**18a**) have been prepared according to ref 19. The thieno[3,4-*b*]pyrazines **20a** and **20b** have been prepared according to ref 20. 2-Phenylfuro[2,3-*b*]quinoxaline (**21a**) and 2-phenylthieno[2,3-*b*]-quinoxaline (**22a**) have been prepared according to ref 21. Quinoxaline and phenazine were obtained from Aldrich Chemical Co.

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Electrolysis of 17a. Preparation of 26a. An electrolysis was carried out at pH 13.1 and E = −1.55 V. The cathodic compartment contained 196 mg (1 mmol) of **1a** in 100 mL of solution (methanol 50%, NaOH 0.1 N 50%). At the end of the electrolysis (2.1 F per mol), methanol was evaporated and the solution was extracted with ether (2 × 100 mL). The etheral solution was dried and then evaporated to give 104 mg of 4,5-dihydro- or 6,7-dihydro-2-phenylfuro[2,3-*b*]pyrazine (**26a**; 52.5% yield): mp 150–152 °C dec; ^{1}H NMR ($CDCl_3$) 5-CH_2 or 6-CH_2, m, 3.0–4.0 ppm (2 H); 5-H or 6-H, m, 5.75–6.00 ppm (1 H); 2-C_6H_5 + 3-H, 2 m, 7.25–7.45 ppm, and 7.75–8.00 ppm (6 H). Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.53; H, 5.20; N, 13.95.

Electrolysis of 26a. Preparation of 27a. An electrolysis was carried out at pH 13.1 and E = −1.55 V. The cathodic compartment contained 196 mg of **1a** in 100 mL of solution (methanol 50%, NaOH 0.1 N 50%). At the end of this first electrolysis the potential was set at E = −1.85 V. After consumption of about 2 F per mol, the methanol was evaporated and the solution was extracted with ether. The etheral solution was dried (Na_2SO_4) and then evaporated to give 72 mg of 4,5,6,7-tetrahydro-2-phenylfuro[2,3-*b*]pyrazine (**27a**; 36% yield): mp 163–165 °C dec; ^{1}H NMR ($CDCl_3$ + D_2O) 5-CH_2 + 6-CH_2, m, 2.7–3.6 ppm (2 H); 3-H + 2-C_6H_5, m centered at 7.25 ppm. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.13; H, 6.15; N, 13.86.

Electrolysis of 18a. Preparation of 29a. An electrolysis was carried out at pH 13.25 and E = −1.45 V. The cathodic compartment contained 212 mg (1 mmol) of **18a** in 100 mL of solution (methanol 50%). At the end of the electrolysis (1.9 F per mol) the precipitate in the cell was filtered under argon, washed with water, and dried to give 150 mg (71% yield) of 4,5- or 6,7-dihydro-2-phenylthieno[2,3-*b*]pyrazine (**29a**): mp 158–160 °C dec; ^{1}H NMR (DMSO-d_6) 5-CH_2 or 6-CH_2, m, 3.0–4.1 ppm (2 H); 5-H or 6-H, m centered at 7.00 ppm (1 H); 2-C_6H_5 + 3-H, m, 7.2–7.75 ppm (6 H). In solution (DMSO-d_6), **29a** is quantitatively oxidized in a few days into **18a** as shown by NMR. Anal. Calcd for $C_{12}H_{10}N_2S$: C, 67.26; H, 4.70; N, 13.07. Found: C, 67.30; H, 4.58; N, 13.16.

Electrolysis of 29a. Preparation of 30a. An electrolysis was carried out at pH 13.2 and E = −1.45 V. The cathodic compartment contained 212 mg of **29a** in 100 mL of solution (methanol 50%). At the end of this first electrolysis the potential was set at E = −1.80 V. After consumption of about 2 F per mol, the methanol was evaporated and the solution was extracted with $CHCl_3$ (2 × 80 mL). The chloroformic solution was dried (Na_2SO_4) and then evaporated. The solid residue (160 mg) was a complex mixture from which was isolated by preparative HPLC (25 cm, 10.5 mm i.d., Sperisorb ODS-2 column eluted with 60/40 methanol/water at 120 mL/h) 85 mg of 4,5,6,7-tetrahydro-2-phenylthieno[2,3-*b*]pyrazine (**30a**): mp 130–132 °C dec; ^{1}H NMR ($CDCl_3$ + D_2O) 5-CH_2 + 6-CH_2, m, 2.8–3.7 ppm (4 H); 3-H + 2-C_6H_5, m, 6.80–7.80 ppm (6 H). Anal. Calcd for $C_{12}H_{12}N_2S$: C, 66.63; H, 5.59; N, 12.95. Found: C, 66.50; H, 5.34; N, 13.05.

Electrolysis of 21a in DMF in the Presence of Acetic Anhydride. Preparation of 33a. The cathodic solution contained 60 mL of solvent, 738 mg (3 mmol) of **21a**, 8 mL of acetic anhydride, and 6 g of tetrabutylammonium iodide, E = −1.5 V. At the end of the electrolysis (i < 3 mA), the catholyte was poured into 200 mL of water. The solid precipitated was filtered, washed with water, and dried to give 795 mg (80% yield) of 4,9-diacetyl-4,9-dihydro-2-phenylfuro[2,3-*b*]quinoxaline (**33a**): mp 83–85 °C dec (hexane); ^{1}H NMR ($CDCl_3$) 4-$COCH_3$ + 9-$COCH_3$, 2 s, 2.50 and 2.60 ppm (3 H + 3 H); 3-H, s, 6.89 ppm (1 H); 5-H + 6-H + 7-H + 8-H + 2-C_6H_5, m, 7.00–8.00 ppm (9 H). Anal. Calcd for $C_{20}H_{16}N_2O_3$: C, 72.27; H, 4.85; N, 8.43. Found: C, 72.25; H, 4.80; N, 8.50.

Electrolysis of 22a in DMF in the Presence of Acetic Anhydride. Preparation of 34a. With the same procedure as for **21a**, 524 mg of **22a** (2 mmol) gives 490 mg (65% yield) of 4,9-diacetyl-4,9-dihydro-2-phenylthieno[2,3-*b*]quinoxaline (**34a**): mp 179–181 °C dec (hexane/benzene = 90/10); ^{1}H NMR ($CDCl_3$) 4-$COCH_3$ + 9-$COCH_3$, 2 s, 2.45 and 2.55 ppm (3 H + 3 H); 3-H;, s, 7.20 ppm (1 H); 5-H + 6-H + 7-H + 8-H + 2-C_6H_5, m, 7.25–7.90 ppm (9 H). Anal. Calcd for $C_{20}H_{16}N_2O_2S$: C, 68.94; H, 4.63; N, 8.04. Found: C, 68.90; H, 4.74; N, 8.11.

Electrolysis of 20a. Preparation of 36a. An electrolysis was carried out at pH 6.85 and E = −0.80 V. The cathodic compartment contained 265 mg of **20a** (1.25 10^{-3} mol) in 100 mL of solution (methanol 50%). At the end of the electrolysis (i < 2 mA; 1.9 F per mol), the methanol was evaporated and the precipitate was filtered, washed with water, and dried to give 218 mg (81.6% yield) of 2,7-dihydro-4-phenylthieno[3,4-*b*]pyrazine (**36a**): mp 88–90 °C dec; ^{1}H NMR ($CDCl_3$) 2-CH_2 + 7-CH_2, s, 4.37 ppm (4 H); 4-C_6H_5, m, 7.37–7.67 and 7.75–8.20 ppm (5 H); 5-H, s, 8.90 ppm (1 H). Anal. Calcd for $C_{12}H_{10}N_2S$: C, 67.26; H, 4.70; N, 13.07. Found: C, 67.41; H, 4.85; N, 12.91.

Electrolysis of 20b. Preparation of 36b. With the same procedure as for **20a** (pH 6.90 and E = −0.85 V) 197 mg of **20b** (1.2 × 10^{-3} mol) gives after evaporation of methanol and extraction with diethyl ether 145 mg (72.5% yield) of 2,7-dihydro-4,5-dimethylthieno[3,4-*b*]pyrazine (**36b**): mp 86–88 °C dec; ^{1}H NMR ($CDCl_3$) 4-CH_3 + 5-CH_3, s, 2.50 ppm (6 H); 2-CH_2 + 7-CH_2, s, 4.19 ppm (4 H). Anal. Calcd for $C_8H_{10}N_2S$: C, 57.80; H, 6.06; N, 16.85. Found: C, 57.91; H, 6.26; N, 16.78.

Hydrogenation of 20a. Preparation of 36a. A catalytic hydrogenation was carried out at room temperature with 110 mg of **20a** in 50 mL of methanol in the presence of 110 mg of 10% Pd/C. After 2 h of stirring and consumption of 1 mol of H_2 per mole of **20a** the solution was filtered and evaporated to give 87 mg (80% yield) of **36a**.

Reduction by $NaBH_4$ of 20a. $NaBH_4$ (200 mg) was added to a solution of **20a** (135 mg) in ethanol (11 mL). After 30 h at 60 °C the mixture was poured in 50 mL of water. Ethanol was evaporated, and the solid that precipitated was filtered, washed with water, and dried to yield 108 mg of **36a** (78% yield).

Reaction of 20a with Methylmagnesium Chloride. Preparation of 37a. A mixture of 212 mg (10^{-3} mol) of **20a**, 1.5 mL of a 3 M solution of CH_3MgCl in tetrahydrofuran (Aldrich) in 10 mL of anhydrous THF was stirred at room temperature for 45 min. The solution was quenched with 10 mL of a 5 M solution of NH_4Cl. The THF was evaporated, and the residue was extracted with ether (200 mL). The etheral solution was dried (Na_2SO_4) and evaporated to give 164 mg (73% yield) of 5,6-dihydro-5-methyl-4-phenylthieno[3,4-*b*]pyrazine (**37a**): mp 86–88 °C; ^{1}H NMR ($CDCl_3$) 5-CH_3, d (J = 7 Hz), 1.25 ppm (3 H); 6-NH, br s, 3.78 ppm (1 H); 5-H, q (J = 7 Hz), centered at 4.70 ppm (1 H); 7-H, d (J = 3 Hz); 6.04 ppm (1 H); 2-H, d, (J = 3 Hz), 7.32 ppm (1 H); 4-C_6H_5, m, 7.40–7.70 and 7.82–8.20 ppm (5 H). Anal. Calcd for $C_{13}H_{12}N_2S$: C, 68.39; H, 5.30; N, 12.27. Found: C, 68.25; H, 5.19; N, 12.21.