N-Substituted 1-Aminoindoles from Electrogenerated *N*-Substituted 2-(*ortho*-Nitrosophenyl)ethylamines

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In memory of Prof. Lydia Rodríguez-Hahn (Instituto de Química, UNAM, México)

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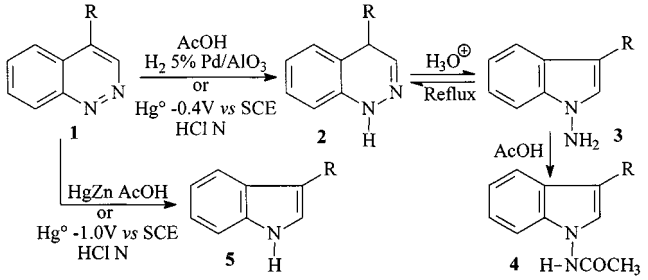
An electrochemical methodology offering efficient access to *N*-alkyl- and *N*-aryl-substituted 1-aminoindoles has been developed. *N*-Substituted 2-(*ortho*-nitrosophenyl)ethylamines, electrogenerated in a "redox" flow cell, undergo intramolecular cyclization to hydrocinnoline-type intermediates. Under slightly basic conditions, these undergo spontaneous ring-contraction to produce the *N*-substituted heterocycles in good yields. The reactions have been studied in slightly acidic and slightly basic aqueous alcoholic media.

Introduction

The synthesis of cinnoline derivatives is an area of interest because of their applications in agricultural, biological,[1] and medical fields.[2] Derivatives of 1,2- and 1,4-dihydrocinnolines are particularly interesting compounds in that they show estrogenic,[3] antiinflammatory,[4] and antibiotic[5] activity. They are also used as substrates in syntheses of other important biologically active heterocyclic compounds (e.g. indoles,[6] 1,3-benzodiazepines[7]).

The 1,4-dihydrocinnolines **2** are usually produced from cinnolines **1** by chemical[4,8,9] or electrochemical[6b] reduction (Scheme 1). However, as a result of ring-contraction and facile reduction of the N−N bond, the indoles **5** are often obtained,[6] and because of hydrogenolysis of the cinnoline substituents,[4] the choice of the reducing agent and experimental conditions are rather limited.



Scheme 1

In hot dilute acid, the 1,4-dihydrocinnolines **2** are in equilibrium with 1-aminoindoles **3**, but the position of the equilibrium depends on the attached substituents.[10] This equilibrium can be shifted in favor of **3** if during the equilibration the primary amine formed is consumed (e.g. by acetylation[6a,11] or by formylation[12]) to form *N*-substituted 1-aminoindoles **4**. The normal procedure for carrying out this derivatization requires extended reaction times and high temperatures. These *N*-substituted heterocycles and their derivatives are interesting compounds owing to their biological activity (as antidepressants[11] and as potential therapeutic agents in combatting Alzheimer's disease[13]) and because of their synthetic utility in heterocyclic chemistry.[14] Considering the traditional methods of synthesis of 1-aminoindoles **3**, the required starting compounds are often difficult to synthesize or the desired functionalization of 1-aminoindole is not easy to achieve, and the yields are at best moderate.[6a,10,13,14c,15,16]

The two-step electrolysis (reduction then oxidation) of 2-(*ortho*-nitrophenyl)ethylamines at a mercury electrode has been carried out in order to synthesize the corresponding nitroso derivatives. The electrophilic character of the electrogenerated nitroso group facilitates generation of the N−N bond of the 1,4-dihydrocinnoline **2** (R = H).[17] Only amines bearing an electron-donating group can be successfully cyclized by this method, because an electron-withdrawing group dramatically decreases the rate of the intramolecular cyclization. Due to the extended time required for the oxidation step at the mercury anode, intermolecular condensation between the hydroxylamino intermediate and the generated nitroso compound can occur, resulting in the formation of azoxy compounds.[18]

Over the past few years, an improved electrochemical "redox" methodology (vide infra) has been developed in this laboratory, whereby nitrosobenzenes can easily be prepared in aqueous alcoholic media at room temperature in excellent yields according to Scheme 2.[19,20] We have used this procedure to synthesize 2-substituted indazoles.[21] This work has now been extended to a study of the cyclization of electrogenerated *N*-substituted 2-(*ortho*-nitrosophenyl)-

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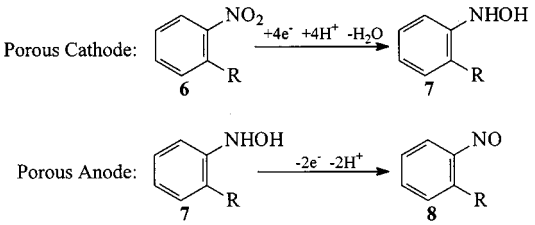
ethylamines and the subsequent ring-contraction of the resulting dihydrocinnolines to furnish *N*-substituted 1-aminoindoles in a one-pot reaction.



Scheme 2

Electroanalytical Studies

Cyclic Voltammetry and Polarography

Electroanalytical studies on ethylamines **6a−f** performed at a glassy carbon electrode in aqueous alcoholic media at various pH values revealed a similar behaviour as that seen with *N*-substituted benzylamines.[21] The electrochemical data from cyclic voltammetric and polarographic analyses of the ethylamines **6a−f** in the studied aqueous alcoholic media are given in Table 1.

At a given pH value, the rate of cyclization depends on the substituent on the ethylamine. As shown by cyclic voltammetry, an electron-withdrawing group decreases the rate of cyclization between the amine and the electrogenerated nitroso group. The "quasi reversible" system observed ($I_a/I_c \approx 1$) at +0.1 to −0.3 V vs. SCE proves that the nitroso group reacts only slowly with the amino group (Figure 1). On the other hand, with an electron-donating substituent the reduction signal of the nitroso compound is not observed (Figure 2), indicating a rapid consumption of the nitroso derivative.

The cyclization rate is also affected by the electrolysis medium. In slightly basic aqueous alcoholic medium, the reversibility of the nitroso-hydroxylamine system of aryl amines is more clearly observed than in slightly acidic aqueous alcoholic media (Figures 1 and 3). Amine **6d** reacts rapidly in acidic aqueous alcoholic media, but only slowly in basic media, where the nitroso-hydroxylamine system can be observed (Table 1, entry **6d**). This behavior can be explained in terms of an acid catalysis of the cyclization reaction between the nitroso group and the amine function, as

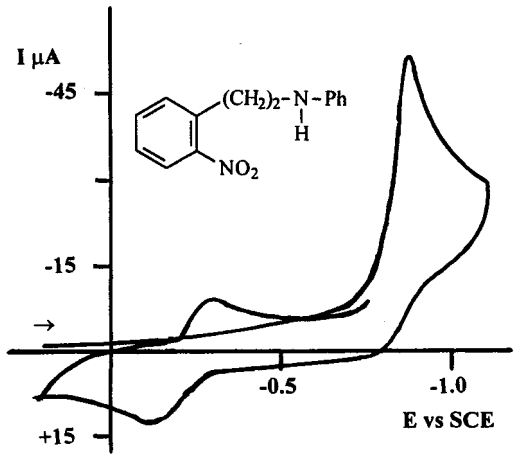


Figure 1. Cyclic voltammetry of **6e**, $2\cdot10^{-3}$ M, GC, 0.1 Vs^{-1}, basic aqueous alcoholic buffer

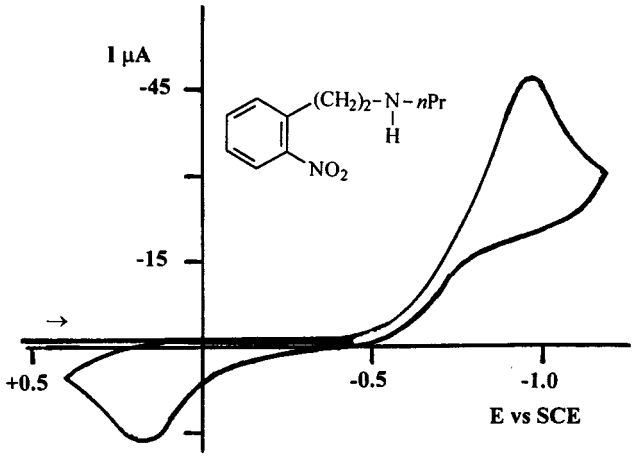
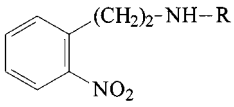


Figure 2. Cyclic voltammetry of **6b**, $2\cdot10^{-3}$ M, GC, 0.1 Vs^{-1}, basic aqueous alcoholic buffer

Table 1. Electrochemical data of *N*-substituted 2-(*ortho*-nitrophenyl)ethylamines **6a−f** in acidic* and basic** media



Ethylamine	$E_{1/2}$*[a]	E_{pc}*[a]	E_{pa}*[b]	E_{pc}*[b]	$E_{1/2}$**[a]	E_{pc}**[a]	E_{pa}**[b]	E_{pc}**[b]
6a R = H	−0.530	−0.825	+0.100	−0.290	−0.670	−0.870	−0.020	≥
6b R = *n*Pr	−0.525	−0.810	+0.200	≥	−0.595	−0.900	+0.150	≥
6c R = CH_2Ph	−0.490	−0.825	+0.250	≥	−0.650	−0.875	+0.080	≥
6d R = $CH(Ph)_2$	−0.463	−0.770	+0.130	≥	−0.675	−0.868	−0.080	−0.290
6e R = Ph	−0.535	−0.850	+0.100	−0.150[v]	−0.685	−0.890	−0.100	−0.300
6f R = Ph(*p*-OMe)	−0.550	−0.790	+0.085	−0.110	−0.695	−0.850	−0.090	−0.275

Polarography: WE = Hg°, τ = 2 s, $c = 2\cdot10^{-3}$ M, V vs. SCE. Cyclic voltammetry: WE = glassy carbon, $v = 0.1$ Vs^{-1}, $c = 2\cdot10^{-3}$ M, V vs. SCE. − * 80% MeOH, 20% aqueous acidic buffer (AcOH/AcONa, 2.5 M). − ** 80% MeOH, 20% aqueous basic buffer (NH_4NO_3/NH_3, 2.5 M). − [a] Reduction signal of nitro group to hydroxylamine derivative. − [b] Redox system of hydroxylamine-nitroso groups. − ≥ Not observed. − [v] Hardly observed at $v = 0.1$ Vs^{-1} but clearly observed at $v > 0.5$ Vs^{-1}.

has previously been observed for other nitrosoaryl condensations.[22] In acidic media, the oxidation peaks of the electrogenerated hydroxylamine derivatives were seen as very broad features at low scan rates ($v < 0.5$ Vs^{-1}). Two very close oxidation systems ($\Delta Ep_a = 0.2$ V) can clearly be observed at higher scan rates.

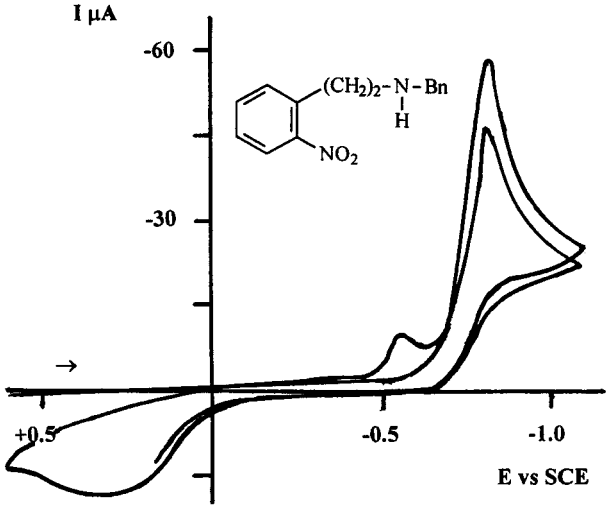


Figure 3. Cyclic voltammetry of **6c**, $2 \cdot 10^{-3}$ M, GC, 0.1 Vs^{-1}, acidic aqueous alcoholic buffer

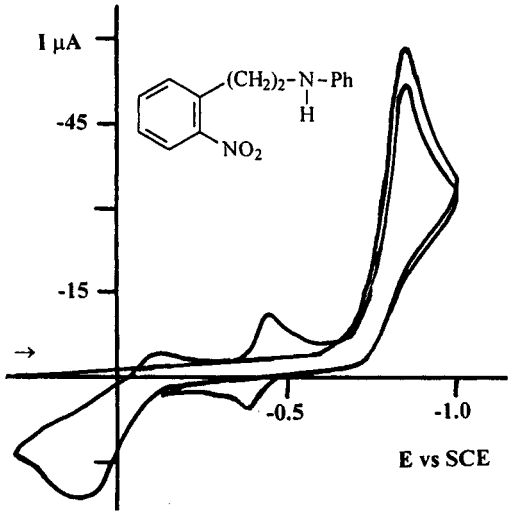


Figure 4. Cyclic voltammetry of **6e**, $2 \cdot 10^{-3}$ M, GC, 0.1 Vs^{-1}, acidic aqueous alcoholic buffer

Cyclic voltammetry of **6** in slightly acidic aqueous alcoholic medium also showed a new wave at the second cathodic sweep. With alkyl substituents, an irreversible system was observed (Figure 3), while with aromatic substituents the system was reversible (Figure 4). The signals intensified with each sweep of the potential, showing an accumulation of the products. We did not observe these peaks in slightly basic aqueous alcoholic media (Figure 5).

The steric effects of the substituent on the *N*-ethylamine affected the rate of cyclization more strongly than in the benzylamine series. In acidic and basic aqueous alcoholic media, we observed the *quasi* reversibility of the nitroso-

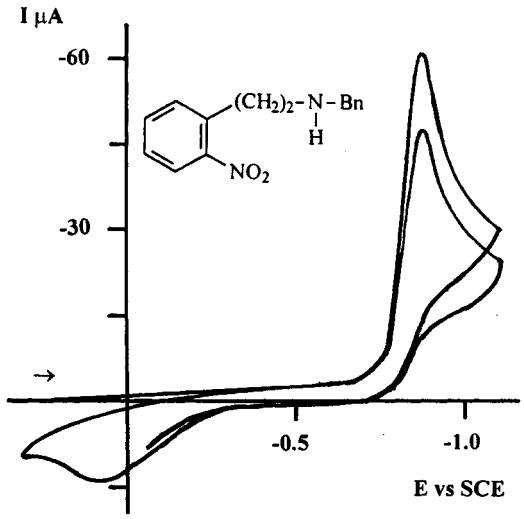


Figure 5. Cyclic voltammetry of **6c**, $2 \cdot 10^{-3}$ M, GC, 0.1 Vs^{-1}, basic aqueous alcoholic buffer

hydroxylamine system with the *N*-aryl-ethylamine **6f** (Table 1, entry **6f**), even though **6f** is an *N*-phenylamine substituted with an electron-donating substituent in the *para* position. On the contrary, the ethylamines bearing a $-CH_2-$ or $-CH-$ group do not show the reduction signal of the electrogenerated nitroso compound (except for **6d** in basic aqueous alcoholic media, vide supra). The importance of steric effects in the course of the intramolecular ring-closure reaction among the members of the *N*-ethylamine series is in accordance with the observed rate of cyclization due to the entropy effect of the transition state: five-membered rings > six-membered rings.[23]

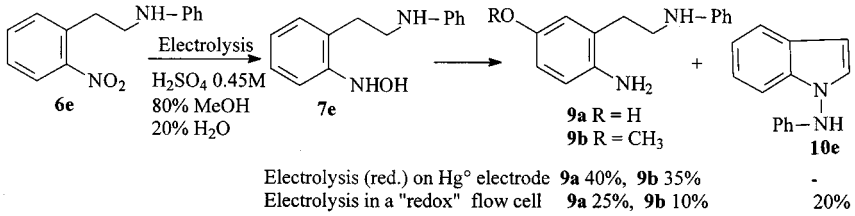
These results show the need for rapid and complete consumption of the hydroxylamine at the anode producing the nitroso derivative, in order to avoid the formation of azoxy compounds.[18]

Macroscale Electrolyses

Electrolyses of Ethylamine 6e in a Strongly Acidic Aqueous Alcoholic Medium (2.5 M aqueous H_2SO_4, MeOH, 1:4, v/v)

First we studied the stability of the hydroxylamine intermediate **7** by controlled-potential electrolysis of **6e** at a mercury cathode (−0.4 V vs. SCE, 4 $Fmol^{-1}$). The polarogram recorded after the electroreduction did not show the reduction wave of the hydroxylamine **7e**. Upon workup of the electrolysis solution, only the aminophenols **9a−b** were isolated (Scheme 3). It is well known that in strongly acidic media arylhydroxylamines can rearrange to aminophenols.[24]

The electrolysis of **6e** in the same medium was also performed in a "redox" flow cell[19,20] fitted with two consecutive porous graphite felt electrodes of opposite polarities (Scheme 2), enabling rapid oxidation at the second porous electrode of the hydroxylamine **7e** produced at the first. A



Scheme 3

mixture of polar products was obtained, from which aminophenols **9a–b** and the unexpected *N*-substituted 1-aminoindole **10e** (discussion vide infra) were isolated in low yields (20%). In view of these results, the strongly acidic medium was not investigated further.

Electrolyses of Ethylamine 6a in Slightly Acidic and Slightly Basic Aqueous Alcoholic Media in a "Redox" Flow Cell

Due to the different behavior of ethylamine **6a**, a separate section is devoted to the results obtained with this compound.

The polarogram recorded after "redox" electrolysis in a flow cell in a slightly acidic aqueous alcoholic medium showed the *quasi* disappearance (> 90% by polarography) of the reduction wave of the nitro group and the appearance of a new cathodic wave ($E_{1/2}$ = −1.35 V vs. SCE). After workup, cinnoline **1** and 1,4-dihydrocinnoline **2** were isolated in yields of 30% and 45%, respectively. A polarographic analysis of the isolated compound **2** showed the same wave as that observed at the end of the electrolysis. The ^{1}H-NMR spectra of **1** and **2** were consistent with the formation of these products.[9b,25] The presence of cinnoline **1** among the isolated products, for which no polarographic wave ($E_{1/2}$ = −0.48 V vs. SCE) could be detected immediately after the electrolysis, can be attributed to aerial oxidation[6] of **2** during the workup.

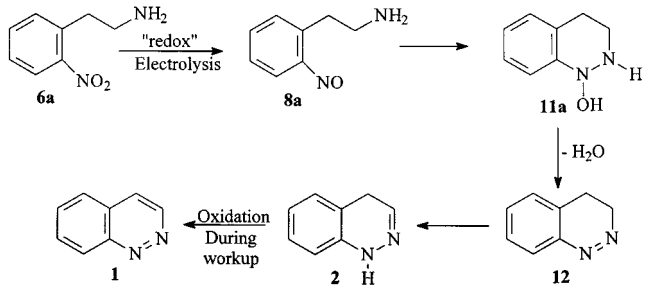
After the "redox" electrolysis of ethylamine **6a** in a slightly basic aqueous alcoholic medium, polarographic analysis showed the wave ($E_{1/2}$ = −0.78 V vs. SCE) for the reduction of intermediate **12**, which rearranges to the 1,4-dihydrocinnoline **2** after a few hours under N_2.[17] After workup, the cinnoline **1** and 1,4-dihydrocinnoline **2** were isolated in yields of 35% and 55%, respectively. The proposed mechanism is shown in Scheme 4.

Electrolyses of Ethylamines 6b–f in Slightly Acidic Aqueous Alcoholic Media (Acetic/Acetate Buffer; AcOH 0.5 mol L^{-1} + AcONa 0.5 mol L^{-1}, MeOH/H_2O, 4:1, v/v) at a Mercury Electrode

We first studied the stabilities of the hydroxylamine and nitroso intermediates **7** and **8** by two-step controlled-potential electrolyses of 2-(*ortho*-nitrophenyl)ethylamines **6b–f** at a mercury electrode (reduction at −0.65 V vs. SCE, 4 $Fmol^{-1}$, then oxidation at 0.1 V vs. SCE, 2 $Fmol^{-1}$). The polarograms recorded after electroreduction showed the anodic waves of the stable hydroxylamines **7b–f** (Figure 6, entry b). The oxidation of hydroxylamines **7b–f** consumed about 3 $Fmol^{-1}$ (theoretical 2 $Fmol^{-1}$). This result is in accordance with the electroanalytical observations, which showed another oxidation system very close to the hydroxylamine oxidation potential.

In the case of *N*-alkyl-ethylamines **6b–d**, the polarogram recorded after reduction followed by oxidation at a mercury electrode showed several cathodic waves corresponding to the irreversible systems seen in the cyclic voltammetry (Figure 6, entry c). The peak potential of the first wave was located at the same potential as the new cathodic system observed during the electroanalyses (vide supra, Figure 4). After workup, we obtained a complex mixture of polar products, from which only the cinnoline **1** and 1,4-dihydrocinnoline **2** could be isolated as major products (Table 2). The expected 2-alkyl-1,4-dihydrocinnolines or 2-alkyl-1,2-dihydrocinnolines were not found in any of these experiments. Polarographic analysis of solutions of isolated **1** and **2** showed the same signals as those observed at the end of electrolysis ($E_{1/2}$ = −0.48 and $E_{1/2}$ = −1.35 V vs. SCE, respectively).

With *N*-aryl-ethylamines **6e–f**, the polarograms recorded after two-step controlled-potential electrolyses at a mercury electrode (reduction then oxidation) showed only one cathodic wave (Figure 8, entry c), corresponding to a revers-



Scheme 4

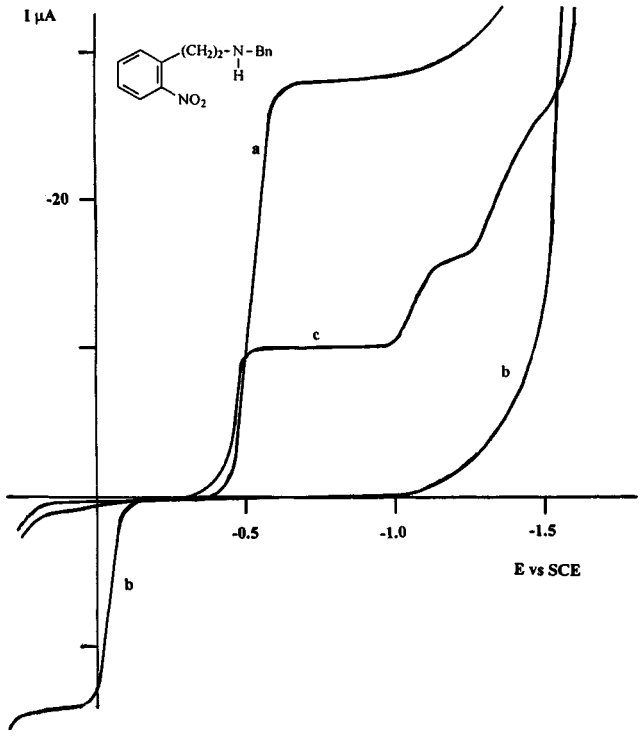


Figure 6. Polarographic control of two-step electrolysis of **6c** at Hg° electrode, $6{\cdot}10^{-3}$ M in slightly acidic aqueous alcoholic medium: a) Solution before electrolysis. b) Solution after reduction at −0.6 V vs. SCE. c) Solution after oxidation at 0.1 V vs. SCE

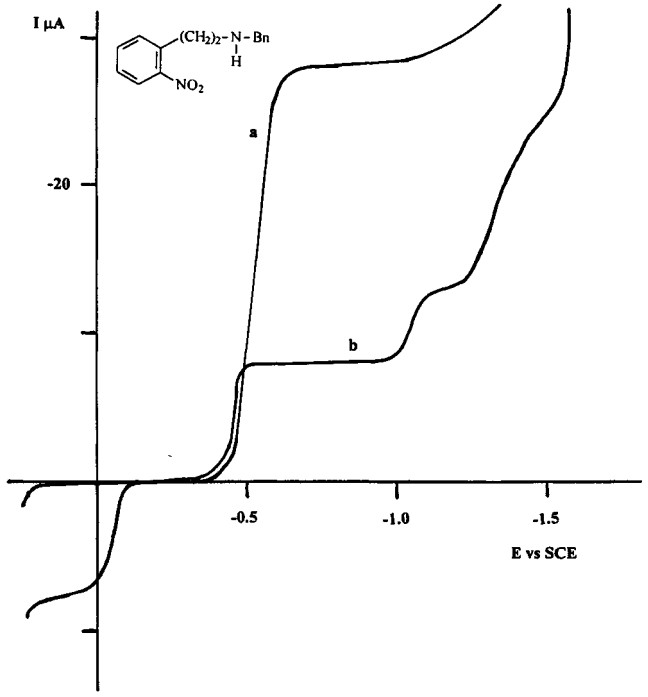


Figure 7. Polarographic control of the "redox" electrolysis of **6c** at porous graphite electrodes, $6{\cdot}10^{-3}$ M in slightly acidic aqueous alcoholic medium: a) Solution before electrolysis. b) Solution immediately after electrolysis

Table 2. Isolated products from *N*-alkylethylamines **6a−d** after "redox" electrolysis in the studied aqueous alcoholic media

Ethylamine	1,4-Dihydrocinnoline **2** (R = H)		Cinnoline **1** (R = H)	
	Acidic buffer	Basic buffer	Acidic buffer	Basic buffer
6a	45%	55%	30%	35%
6b	25%	7%	53%	25%
6c	19%	6%	50%	28%
6d	10%	4%	55%	15%

ible system (Figure 8, entry d) located at the same potential as that of the system observed by cyclic voltammetry of the starting compound (Figure 4). After workup of the electrolysis solutions, we isolated the *N*-substituted 1-aminoindoles **10e−f** as major products, albeit in low yields (28 and 38%, respectively), and complex mixtures of unidentified products.

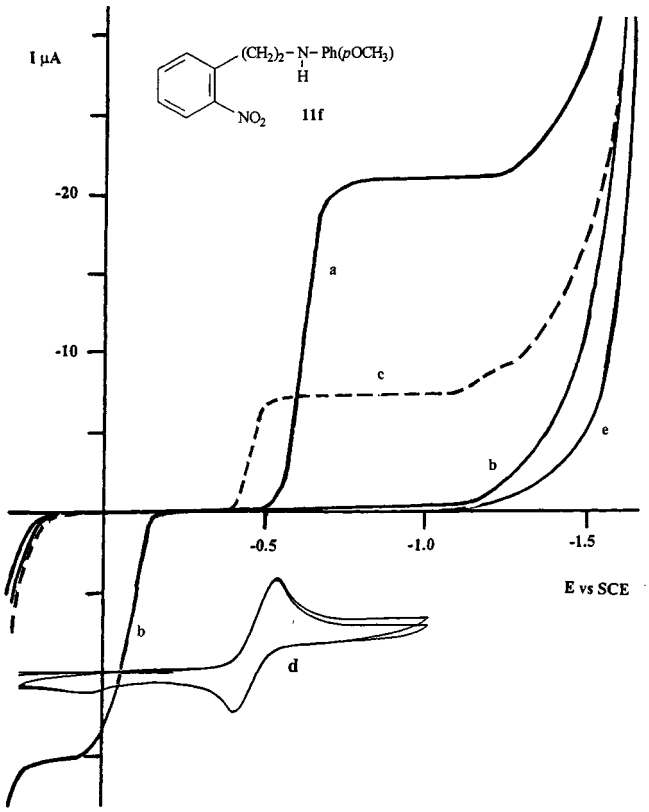


Figure 8. Polarographic control of the three-step "redoxred" electrolysis of **6f** on an Hg° electrode, $6{\cdot}10^{-3}$ M in slightly acidic aqueous alcoholic medium: a) Solution before electrolysis. b) Solution immediately after first electroreduction at −0.7 V vs. SCE. c) Solution after electrooxidation at 0.1 V vs. SCE. d) Cyclic voltammetry of the solution after electrooxidation at 0.1 V vs. SCE, GC, $v = 0.1\ Vs^{-1}$. e) Solution immediately after second electroreduction at −0.6 V vs. SCE

The ^{1}H-NMR spectra of the *N*-substituted 1-aminoindoles **10e−f** showed the signals of 2-H and 3-H as an AB system with ^3J = 3.3 Hz, as well as long-range coupling (^5J = 0.9 Hz) between 3-H and 7-H, typical of an indole ring.[26] An X-ray structure analysis of **10f** confirmed the structure of the isolated compound (Figure 9). Neither 1,4-

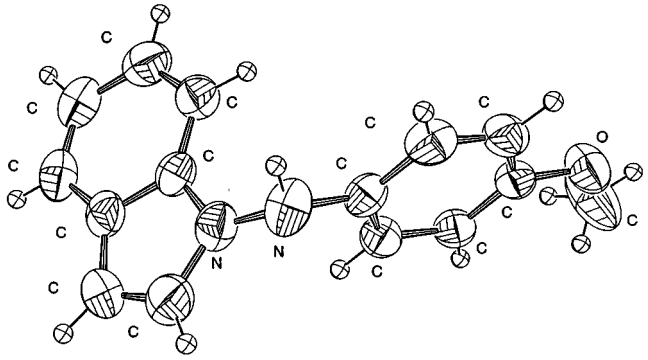


Figure 9. Crystal structure of **10f**

dihydrocinnoline **2** nor cinnoline **1** were isolated alongside these compounds.

The intermediate showing a reversible system decomposed during workup, leading to a complex mixture of polar products. Consequently, we performed a three-step electrolysis at a mercury electrode. After reduction (4 $Fmol^{-1}$) of the *N*-aryl-ethylamines **6e−f** followed by oxidation (3 $Fmol^{-1}$), we finally reduced the oxidized form of the electrogenerated reversible system (1.3 $Fmol^{-1}$ were consumed). The polarograms recorded during the electrolyses of **6f** are shown in Figure 8. After workup, the *N*-substituted 1-aminoindoles **10e−f** were isolated in 80−85% yield.

Electrolyses of Ethylamines 6b−f in Slightly Acidic Aqueous Alcoholic Media (Acetic/Acetate Buffer, AcOH 0.5 mol L^{-1} + AcONa 0.5 mol L^{-1}, MeOH/H_2O, 4:1, v/v) in a "Redox" Flow Cell

Following electrolyses of *N*-alkylethylamines **6b−d** in the "redox" flow cell, we observed the *quasi* disappearance of the reduction wave of the nitro group (Figure 7b) and the presence of the same cathodic waves as previously characterized following the two-step electrolyses at a mercury electrode. Moreover, the hydroxylamines **7b−d** were not totally oxidized with the theoretical quantity of electricity (2 $Fmol^{-1}$). This observation confirms the results of the two-step electrolyses at a mercury electrode, where 3 $Fmol^{-1}$ were consumed during the electrooxidation step. The use of a "redox" flow cell with two counterelectrodes and three electrical circuits (upstream and downstream), so as to increase the anodic current to 3 $Fmol^{-1}$,[27] led to the disappearance of the hydroxylamine wave without a change in the profile of the cathodic waves. After workup of the electrolysis solutions, the same complex mixtures of polar products as those generated in the two-step electrolyses at a mercury electrode were obtained, from which only cinnoline **1** and 1,4-dihydrocinnoline **2** could be isolated, in almost the same yields as before (Table 2).

Moreover, benzophenone was isolated as a by-product (yield 35%) following "redox" electrolysis of **6d** in the flow cell. In order to dismiss the hypothesis that benzhydrol was oxidized to benzophenone by the nitroso intermediate, we verified by polarography that a mixture of *o*-nitrosotoluene and benzhydrol does not react under the electrolysis conditions. Thus, the polarographic wave ($E_{1/2}$ = −1.1 to −1.2 V vs. SCE) corresponds to the C=O reduction of the carbonyl compound (benzaldehyde) formed during the electrolysis (Figure 7b). A polarographic study of *ortho*-nitrosotoluene and 1,4-dihydrocinnoline **2** under the electrolysis conditions showed that **2** can be oxidized during the electrolysis by the electrogenerated nitroso derivative **8** to produce the cinnoline **1**. Therefore, the oxidation of **2** to the isolated cinnoline **1** can occur either during the electrolysis or the workup (vide supra).

With *N*-aryl-ethylamines **6e−f**, the polarograms recorded after the "redox" electrolysis in a flow cell showed the *quasi* total disappearance of the cathodic wave of the nitro compound. As with the *N*-alkyl-substituted derivatives **6b−d**, we observed incomplete oxidation of hydroxylamines **7e−f** at the porous anode after passage of the theoretical quantity of electricity (2 F mol^{-1}). These results are again in accordance with the 3 $Fmol^{-1}$ consumed during oxidation at a mercury anode in the two-step electrolyses. The same reversible system as that observed after two-step electrolyses at a mercury electrode (Figure 8) was also present at the end of "redox" electrolyses in the flow cell. Moreover, the isolated products and the yields were almost the same in the two experiments. The use of a "redox" flow cell with two counterelectrodes and three electrical circuits, so as to increase the anodic current to 3 $Fmol^{-1}$,[27] led to the disappearance of the anodic wave of hydroxylamine and an increase in the reversible system signal. After workup, slightly improved yields of **10e−f** were obtained (+10%).

In order to reproduce the three-step electrolyses performed at a mercury electrode, we used a "red-ox-red" flow cell with three consecutive porous electrodes, based on the same principles as the previously described flow cell (Figure 10).[19,20] After electrolyses of *N*-aryl-ethylamines **6e−f** in the "redoxred" flow cell (reduction 4 $Fmol^{-1}$, oxidation 3 $Fmol^{-1}$, then reduction 1 $Fmol^{-1}$), polarograms of the outlet solutions showed the *quasi* total disappearance of the anodic and cathodic waves. After workup, **10e−f** were isolated in 65% yield without optimization of the current intensities.

Electrolyses of *N*-Substituted Ethylamine 6e in Slightly Basic Aqueous Alcoholic Medium (Ammonia/Ammonium Buffer, NH_4NO_3 0.5 mol L^{-1} + NH_4OH 0.5 mol L^{-1}, MeOH/H_2O, 4:1, v/v) at a Mercury Electrode

The polarogram recorded after the two-step controlled-potential electrolysis (reduction then oxidation) of *N*-substituted ethylamine **6e** at a mercury electrode in a slightly basic aqueous alcoholic medium showed the complete oxidation of hydroxylamine **7e** after passage of only 60% of the theoretical quantity of electricity (1.2 $Fmol^{-1}$ instead of 2 $Fmol^{-1}$). At the end of the electrolysis, the polarogram showed only a reducible system ($E_{1/2}$ = −1.01 V vs. SCE). After workup, the azoxy compound **13** (35% yield) and the

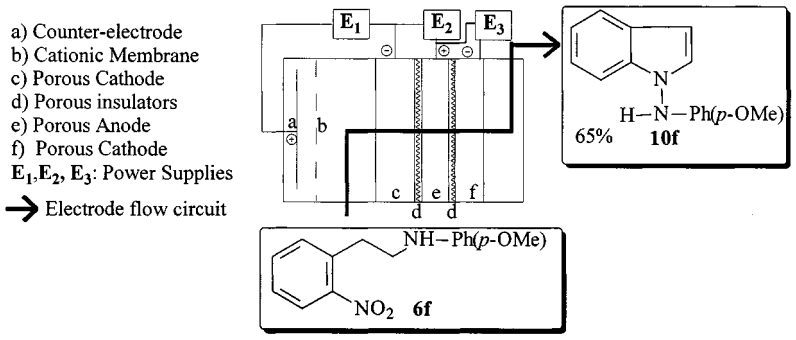
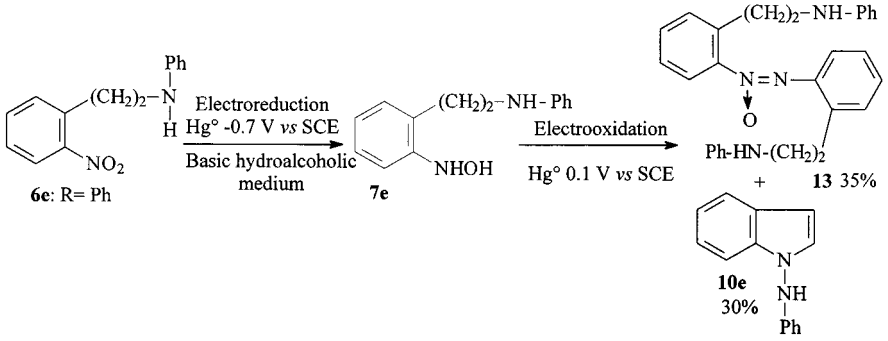


Figure 10. "Redoxred" flow cell with three porous graphite felt electrodes of alternating polarities



Scheme 5

N-substituted 1aminoindole **10e** (30% yield) were isolated (Scheme 5).

Electroanalytical studies on isolated **13** showed the typical signals for an azoxy compound, which matched those observed at the end of the electrolysis. These results are in accordance with the quantity of electricity passed during the oxidation in that a part of the hydroxylamine **7e** was consumed by reaction with an equivalent of the nitroso compound **8e** to form an azoxy compound. This reaction can be avoided by using a "redox" flow cell.

Electrolyses of Ethylamines 6b−f in Slightly Basic Aqueous Alcoholic Media (Ammonia/Ammonium Buffer, NH_4NO_3 0.5 mol L^{-1} + NH_4OH 0.5 mol L^{-1}, MeOH/H_2O, 4:1, v/v) in a "Redox" Flow Cell

The polarogram recorded after the "redox" electrolysis of the *N*-substituted ethylamine **6e** performed in slightly basic aqueous alcoholic medium showed the *quasi* disappearance (> 90% by polarography) of the reduction wave of the nitro compound (Figure 11, entry a). The hydroxylamine **7e** formed at the first electrode was *quasi* totally oxidized with the theoretical amount of electricity (2 $Fmol^{-1}$) at the second electrode, so as to form the nitroso derivative **8e**. Characteristic features of nitroso compounds[28] were in evidence: a two-electron reduction signal ($E_{1/2}$= −0.22 V vs. SCE) and a strong yellow color of the solution (Figure 11, entry b).

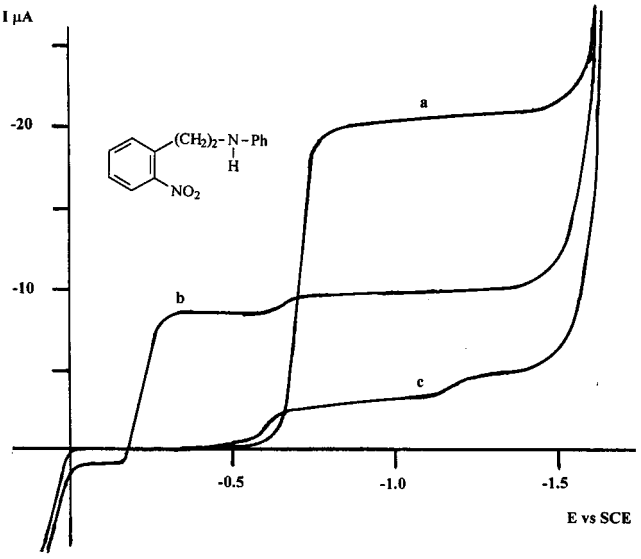


Figure 11. Polarographic control of the "redox" electrolysis of **6e**, $6{\cdot}10^{-3}$ M in slightly basic aqueous alcoholic medium: a) Solution before electrolysis. b) Solution after electrolysis. c) Solution after 3 h under N_2

It was not necessary to isolate the electrogenerated nitroso derivative **8e**. Within a few hours under nitrogen at room temperature, the electrogenerated nitroso group

underwent an intramolecular reaction with the amino group, in the reservoir of the outlet solution. The completion of the cyclization was indicated by the disappearance of the reduction wave of the nitroso group (Figure 11, entry c). After workup, the *N*-substituted 1-aminoindole **10e** was isolated in 65% yield. In this medium we obtained the best yield for the synthesis of **10e** and the least amount of by-products. Thus, we used this medium for the synthesis of 1-aminoindoles **10b−f** (Table 3).

Table 3. Yields of 1,4-dihydrocinnoline **2** and *N*-substituted 1-aminoindoles **10b−f** from "redox" electrolyses of *N*-substituted 2-(*o*-nitrophenyl)ethylamines **6b−f** in the studied media

Ethylamine	Product (Isolated)	Acidic medium	Basic medium
6b R = *n*Pr	**10b**	–	25%
6c R = CH_2Ph	**10c**	–	60%
6d R = $CH(Ph)_2$	**10d**	–	71%
6e R = Ph	**10e**	28%	62%
6f R = Ph(*p*-OMe)	**10f**	38%	62%

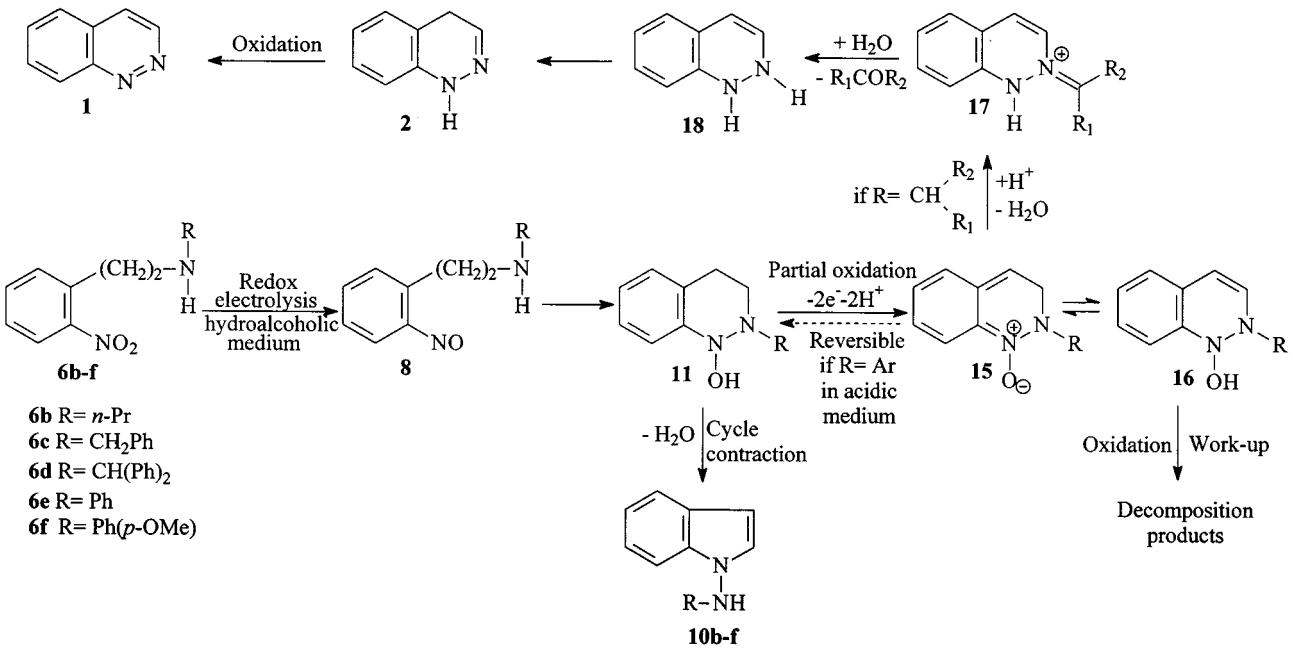
For derivatives **6b−c**, bearing electron-donating, non sterically hindering *N*-substituents, the rate of cyclization was fast and the polarographic wave of the nitroso compound **8** was not observed upon analysis of the outlet solution. The *N*-alkyl-1-aminoindoles **10b−d** were produced in acceptable yields (25−70%). Cinnoline **1** and 1,4-dihydrocinnoline **2** were isolated as by-products (5−20%, Table 2). The compounds **10b−d** showed the typical ^{1}H-NMR signals of the indole ring, as also observed for the *N*-aryl-1-aminoindoles **10e−f** (vide supra). Moreover, we clearly observed the coupling (^3J = 2−3.9 Hz) of the N−H hydrogen with the vicinal alkyl hydrogens. This coupling disappears when the N−H is allowed to exchange with D_2O. The structures were confirmed by acetylation of *N*-benzyl-1-aminoindole **10c**, which produced the acetylated product **14** in 70% yield. The ^{1}H-NMR spectrum of this *N*-acetyl-*N*-benzyl-1-aminoindole **14** showed an AB system (^2J = 14.2 Hz) for the diastereotopic $-CH_2-$ hydrogens and a loss of coupling with the N−H group. We observed the singlet signal of the acetyl group at δ = 1.77. No other change in the profile of ^{1}H-NMR signals was observed.

Discussion

The mechanism proposed in Scheme 6 accounts for the experimental results obtained following electrolyses of ethylamines **6b−f** in slightly acidic and slightly basic media.

In slightly basic media, the nitroso derivatives **8e−f** slowly cyclize. Due to the extended time required for anodic oxidation at a mercury electrode, large amounts of azoxy compounds are produced. Using the redox flow cell, however, the nitroso derivatives leave the porous anode without undergoing cyclization; the *N*-hydroxy intermediates **11e−f** are formed, which rearrange in the outlet solution to give *N*-aryl-1-aminoindoles **10e−f**.

In slightly acidic media, the cyclization of **8e−f** is faster than in basic media owing to an acid catalysis and a part of the *N*-hydroxy intermediates **11e−f** produced are oxidized at the anode (graphite felt or mercury electrode) to give the reducible species **15e−f**. These species are stable in solution in the absence of air, probably due to the possibility of resonance stabilization of the positive charge in the aromatic ring. The intermediates **11e−f** can be regenerated by a second reduction at the mercury cathode or at the third porous electrode of the "redoxred" flow cell (Figure 10), thereby increasing the yield of *N*-aryl-1-aminoindoles **10e−f**.



Scheme 6

In slightly acidic media, the fast cyclization of nitroso derivatives **8b−d** occurs at the anode (mercury or graphite felt) leading to the *N*-hydroxy intermediates **11b−d**. These intermediates are immediately oxidized to the unstable compounds **15b−d**, which rearrange into the iminium intermediates **17b−d**. Hydrolysis of **17b−d** gives a carbonyl compound (aldehyde or ketone) and the 1,4-dihydrocinnoline **2**, which can be oxidized to cinnoline **1** during workup or under the conditions of the electrolysis.

In slightly basic media, the stability of nitroso derivatives **8b−d** is higher than in acidic media, thus only a part of **8b−d** undergoes cyclization at the anode to **11b−d**, giving **15b−d** and the corresponding hydrolysis products (**2** and **1**) as by-products (vide supra). The remainder of the **8b−d** cyclizes after leaving the anode, leading to intermediates **11b−d**, ring-contraction of which gives the *N*-alkyl-1-aminoindoles **10b−d**.

Conclusion

The efficiency of the "redox" process in the smooth electrochemical preparation of aromatic nitroso compounds from the corresponding nitro compounds, without coupling to form azoxy derivatives, has allowed us to synthesize the *N*-substituted 1-aminoindoles **10** in acceptable yields (25−71%). The electrochemical procedure is a general method that employs readily obtainable products (2 steps from commercial products) and tolerates a wide range of *N*-substituents. Only the low-yielding five-step synthesis of *N*-(*n*-propyl)-1-aminoindole **10b** from indole has been described previously.[13] Basic aqueous alcoholic media appear to be of most interest for the synthesis of the *N*-substituted 1-aminoindoles **10** in a "redox" flow cell. Only with the 2-(*ortho*-nitrophenyl)ethylamine **6a** was it possible to synthesize the expected 1,4-dihydrocinnoline **2** without ring-contraction. This methodology overcomes limitations of conditions, time, and yield associated with chemical preparations of *N*-substituted 1-aminoindoles. Further mechanistic investigations are in progress aimed at clarifying the ring-contraction pathway.

Experimental Section

General: Melting points were determined using a Kofler apparatus and are uncorrected. − IR spectra were recorded on a Nicolet 205 FT-IR instrument (in KBr). − NMR spectra were determined for solutions in deuteriochloroform with TMS as internal reference and obtained on a Bruker DPI 200 FT spectrometer operating at 200 MHz (^{1}H) and 50 MHz (^{13}C). − Mass spectra were obtained on a Varian MAT 311 high-resolution mass spectrometer. − Elemental analyses, obtained only for the new compounds, were performed at the Service Central d'Analyse, Département Analyse Elémentaire CNRS (Vernaison). − Thin-layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel (Macherey−Nagel Alugram Sil G/UV^{254}). Column chromatography was performed on silica gel (Acros 0.030−0.075 mm). − Reagents were purchased from Aldrich Chemical Co. or Acros Chemical Co. and used without prior purification.

The starting *N*-substituted 2-(*ortho*-nitrophenyl)ethylamines **6** were readily prepared (global yield 75−85%) by BH_3 reduction[29] of the amides obtained by condensation of *ortho*-nitrophenylacetyl chloride with the appropriate primary amines.[30] All compounds **6** gave satisfactory IR and ^{1}H-NMR spectra and were used without further purification.

Electrochemical Instrumentation and Procedures: Conventional electrochemical equipment was used for polarography, cyclic voltammetry, and controlled-potential electrolyses (EG&G Princeton Applied Research model 362 scanning potentiostat with an XY recorder). Controlled-potential electrolyses were performed at a mercury pool cathode, under nitrogen atmosphere, in a cell described previously.[31] Coulometric measurements were made with a Tacussel model IG 5 N current integrator. "Redox" electrolyses were performed at controlled current, under nitrogen atmosphere, in a flow cell as described previously.[19,20] Two working electrodes (5.2 cm diameter, 12 mm thickness for cathode and 6 mm thickness for anode) were made of graphite felt (Le Carbone Lorraine). The cell was run with two power supplies 0−30 V/3 A. The current intensities were calculated from Faraday's law; for the same current intensities in the two electrical circuits, the cathodic current is twice the anodic intensity. Electrolyses were monitored by polarography (scan rate: 5 mVs^{-1}; drop time *t*: 2 s).

General Procedure for Preparative Controlled-Potential Electrolyses (Two-Step Electrolyses) at a Mercury Electrode: The *N*-substituted 2-(*ortho*-nitrophenyl)ethylamines **6** (3−4 mmol) were dissolved in a mixture (100−150 mL) of acetic/acetate buffer (AcOH 2.5 mol L^{-1} + AcONa 2.5 mol L^{-1}) and methanol (1:4, *v/v*), or of ammonia/ammonium buffer (NH_4NO_3 2.5 mol L^{-1} + NH_3 2.5 mol L^{-1}) and methanol (1:4, *v/v*). Nitrogen was then bubbled through the resulting solution for 10 min. Electrolysis was performed under nitrogen at controlled potential: first at −1.0 to −1.2 V vs. SCE for nitro group reduction, and then at 0.0 to 0.15 V vs. SCE for hydroxylamine oxidation. The electrolysis was directly monitored in the cell by polarography. After complete disappearance of the relevant waves, the electrolysis was stopped. The aqueous/organic mixture was separated from the mercury and the methanol was removed in vacuo in a rotary evaporator. With acidic aqueous alcoholic media, the solution was first neutralized (pH 7−8) with $NaHCO_3$. The reaction mixture was then extracted with CH_2Cl_2 (4 × 30 mL). The organic fraction was dried with $MgSO_4$ and concentrated by rotary evaporation. The crude reaction products obtained were purified by medium-pressure column chromatography.

General Procedure for Preparative "Redox" Electrolyses in the Flow Cell: *N*-Substituted 2-*(ortho*-nitrophenyl)ethylamine **6** (3−9 mmol) was dissolved in a mixture (500−1000 mL) of aqueous alcoholic buffer solution (vide supra). Nitrogen was bubbled through this solution for 30 min prior to the electrolysis. The solution was pumped through the cell from a reservoir using a peristaltic pump. The flow rate (4.8−5.2 mL min^{-1}) was measured from the outlet solution. The current intensities ($I_1 = I_2$) were calculated from Faraday's law according to the quantity of substrate flowing through the porous electrodes per second.[19,20] The efficiencies of the electrolyses were monitored directly by polarography in the reservoir of the outlet solution. After complete disappearance of the nitroso reduction wave, the methanol was removed in vacuo in a rotary evaporator. With acidic aqueous alcoholic media, the solution was first neutralized (pH 7−8) with $NaHCO_3$. The reaction mixture was then extracted with CH_2Cl_2 (4 × 30 mL). The organic fraction was dried with $MgSO_4$ and concentrated by rotary evaporation. The crude reaction products obtained were purified by medium-pressure column chromatography.

General Procedure for Preparative "Redoxred" Electrolysis in the Flow Cell: *N*-(*para*-Methoxyphenyl)-2-(*ortho*-nitrophenyl)ethylamine **6f** (3 mmol) was dissolved in a mixture (500 mL) of acetic/acetate buffer (AcOH 2.5 mol L^{-1} + AcONa 2.5 mol L^{-1}) and methanol (1:4, *v/v*). Nitrogen was then bubbled through this solution for 30 min prior to the electrolysis. The solution was pumped through the cell from a reservoir using a peristaltic pump. The flow rate (4.8−5.2 mL min^{-1}) was measured from the outlet solution. The current intensities ($I_1 = I_2 = 2I_3$) were calculated from Faraday's law according to the quantity of substrate flowing through the porous electrodes per second.[19,20] The efficiencies of the electrolyses were monitored directly by polarography in the reservoir of the outlet solution. The methanol was removed in vacuo in a rotary evaporator and the remaining solution was neutralized (pH 7−8) with $NaHCO_3$. The mixture was then extracted with CH_2Cl_2 (4 × 30 mL). The organic fraction was dried with $MgSO_4$ and concentrated by rotary evaporation. The crude reaction products obtained were purified by medium-pressure column chromatography.

Cinnoline (**1**): After "redox" electrolysis of 2-(*ortho*-nitrophenylethyl)propylamine **6b** (1.65 g, 9 mmol) in 600 mL of acetic/acetate buffer solution and subsequent separation by column chromatography (petroleum ether/EtOAc, 50:50), cinnoline **1** was obtained as a brown oil (lit. brown oil[32]); 0.64 g, 55%. − IR (KBr): $\tilde{\nu}$ = 3057, 1581, 1492, 1417, 1298, 1392, 1138, 1091, 845, 749, cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 9.25 (d, *J* = 5.9 Hz, 1 H, 3-H), 8.44 (dm, *J* = 7.6 Hz, 1 H, 8-H), 7.8−7.6 (m, 4 H, 7-H, 6-H, 5-H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 150.5, 144.7, 131.0, 130.5, 129.4, 126.4, 125.8, 122.5. − HRMS (EI, 70 eV); *m/z* (%): 131 (9.23) [M^+ + 1], 130.0530 (100) [M^+], 102 (65.1), 76 (38.8), 75 (11.6), 74 (9.4), 63 (7.4), 51 (12.7), 50 (22.3) 28 (13); $C_8H_6N_2$ requires [M^+] at 130.0531.

1,4-Dihydrocinnoline (**2**): After "redox" electrolysis of 2-(*ortho*-nitrophenyl)ethylamine **6a** (1.65 g 9 mmol) in 600 mL of acetic/acetate buffer solution and subsequent separation by column chromatography (petroleum ether/EtOAc, 80:20), **2** was recrystallized from petroleum ether/diethyl ether and was obtained in the form of brown crystals; m.p. 81−82°C (lit. 81−82.5°C[9b]); 0.56 g, 45%. − IR (KBr): $\tilde{\nu}$ = 3306, 1602, 1468, 1434, 1298, 1252, 1191, 1036, 1014, 825, 790, 749, 706 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.65 (s, 1 H, exch.-D_2O, N−H), 7.12 (ddd, *J* = 8.7, 6.7, 2.4 Hz, 1 H, 7-H), 7.05−6.9 (m, 2 H, 6-H, 5-H), 6.76 (t, *J* = 2.9 Hz, 1 H, 3-H), 6.66 (d, *J* = 7.8 Hz, 1 H, 8-H), 3.31 (d, *J* = 2.9 Hz, 2 H, CH_2). − ^{13}C NMR ($CDCl_3$): δ = 140.0, 136.1, 127.5, 126.9, 122.5, 115.0, 111.8, 27.1. − HRMS (EI, 70 eV); *m/z* (%): 132.0688 (54) [M^+], 131 (100) [M^+ − 1], 104 (5.52), 77 (22), 66 (4.2), 51 (13.7), 39 (4.7); $C_8H_8N_2$ requires [M^+] at 132.0687.

***meta*-(Anilinoethyl)-*para*-aminophenol** (**9a**): After reduction of 2-(*ortho*-nitrophenyl)-*N*-phenylethylamine **6e** (0.6 g, 2.4 mmol) in 150 mL of 0.5 M H_2SO_4 solution (MeOH/H_2O, 4:1) in a mercury electrode batch cell, followed by workup and separation by medium-pressure column chromatography (petroleum ether/ethyl acetate, 70:30), aminophenol **9a** was isolated as a white, crystalline product (m.p. 131−132°C); 0.220 g, 40%. − IR (KBr): $\tilde{\nu}$ = 3392, 3351, 3289, 3044, 2921, 1598, 1507, 1455, 1381, 1319, 1218, 963, 946, 860, 750 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.45 (br. s, 1 H, exch.-D_2O, OH), 7.1−6.95 (m, 2 H), 6.65−6.4 (m, 6 H), 4.85 (br. s, 1 H, exch.-D_2O, NH), 3.95 (br. s, 2 H, exch.-D_2O, NH_2), 3.31 (br. t, *J* = 7.4 Hz, 2 H, CH_2), 2.72 (t, *J* = 7.4 Hz, 2 H, CH_2).

***ortho*-(Anilinoethyl)-*para*-methoxyaniline** (**9b**): After reduction of 2-(*ortho*-nitrophenyl)-*N*-phenylethylamine **6e** (0.6 g, 2.4 mmol) in 150 mL of 0.5 M H_2SO_4 solution (MeOH/H_2O, 4:1) in a mercury electrode batch cell, followed by workup and separation by medium-pressure column chromatography (petroleum ether/ethyl acetate, 70:30), *p*-methoxyaniline **9b** was isolated as a colourless oil; 0.150 g, 35%. − IR (KBr): $\tilde{\nu}$ = 3401, 3362, 3014, 2936, 1602, 1504, 1431, 1320, 1240, 1158, 1050, 752, 694 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.3−7.15 (m, 2 H), 6.85−6.60 (m, 6 H), 3.78 (s, 3 H, OCH_3) 3.6 (br. s, 3 H, exch.-D_2O, NH and NH_2), 3.42 (t, *J* = 6.8 Hz, 2 H, CH_2), 2.75 (t, *J* = 6.8 Hz, 2 H, CH_2).

***N*-Propyl-1-aminoindole** (**10b**): After "redox" electrolysis of *N*-(*ortho*-nitrophenylethyl)propylamine **6b** (1.5 g, 7.2 mmol) in 1000 mL of ammonia/ammonium buffer solution and subsequent separation by column chromatography (petroleum ether/acetone, 96:4), the indole **10b** was obtained as an orange oil (lit. yellow oil[13]); 0.315 g, 25%. − IR (KBr): $\tilde{\nu}$ = 3301, 3051, 2960, 2933, 2874, 1510, 1450, 1322, 1215, 760, 741 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.68 (dd, *J* = 7.8, 0.8 Hz, 1 H, 7-H), 7.5 (d, *J* = 8.1 Hz, 1 H, 4-H), 7.35−7.1 (m, 3 H, 2-H, 4-H, 5-H), 6.48 (dd, *J* = 3.3, 0.8 Hz, 1-H, 3-H), 4.8 (s, 1 H, exch.-D_2O, N−H), 3.17 (br. t, *J* = 6.2 Hz, 2 H, CH_2), 1.53 (sextet, *J* = 7.3 Hz, 2 H, CH_2), 1.02 (t, *J* = 7.4 Hz, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 135.5, 127.6, 126.3, 121.5, 120.9, 119.5, 109.1, 99.1, 53.7, 21.2, 11.3. − HRMS (EI, 70 eV); *m/z* (%): 175 (13.2) [M^+ + 1], 174.1159 (100) [M^+], 173 (15.77) [M^+ − 1], 145 (27), 132 (16.3), 131 (99.8), 118 (36.3), 117 (60.4), 116 (95.2), 104 (12.3), 90 (17.3), 99 (24.1), 77 (17.1), 63 (17.7), 51 (7.7), 39 (6.7); $C_{11}H_{14}N_2$ requires [M^+] at 174.1156. − $C_{11}H_{14}N_2$: calcd. C 75.82, H 8.10, N 16.08; found C 75.76, H 8.11, N 15.82.

***N*-Benzyl-1-aminoindole** (**10c**): After "redox" electrolysis of 2-(*ortho*-nitrophenyl)-*N*-benzylethylamine **6c** (1.5 g, 5.8 mmol) in 1000 mL of ammonia/ammonium buffer solution and subsequent separation by column chromatography (petroleum ether/diethyl ether, 94:6), the indole **10c** was obtained as an orange oil; 0.77 g, 60%. − IR (KBr): $\tilde{\nu}$ = 3293, 3063, 3028, 2924, 1604, 1496, 1453, 1318, 1215, 1081, 748, 716, 427 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.76 (dd, *J* = 7.7, 0.7 Hz, 1 H, 7-H), 7.6 (d, *J* = 8 Hz, 1 H, 4-H), 7.5−7.2 (m, 7 H, 5-H, 6-H, 2′-H, 3′-H, 4′-H), 7.15 (d, *J* = 3.3 Hz, 1 H, 2-H), 6.52 (dd, *J* = 3.3, 0.7 Hz, 1 H, 3-H), 5.01 (br. t, 1 H, exch.-D_2O, N−H), 4.36 (d, *J* = 3.9 Hz, 2 H, CH_2). − ^{13}C NMR ($CDCl_3$): δ = 136.9, 135.1, 128.8, 128.4, 127.7, 126.4, 121.6, 120.9, 119.6, 108.9, 99.1, 56.06. − HRMS (EI, 70 eV); *m/z* (%): 223 (9.1) [M^+ + 1], 222.1149 (47.3) [M^+], 132 (14.2), 131 (100), 117 (15.3), 104 (12.2), 91 (22.6), 99 (20.4), 78 (8.6), 77 (18.6), 65 (8.2), 39 (7); $C_{15}H_{14}N_2$ requires [M^+] at 222.1156. − $C_{15}H_{14}N_2$: calcd. C 81.05, H 6.35, N 12.60; found C 80.98, H 6.67, N 12.54.

***N*-(*C*,*C*-Diphenylmethyl)-1-aminoindole** (**10d**): After "redox" electrolysis of 2-(*ortho*-nitrophenyl)-*N*-(*C*,*C*-diphenylmethyl)ethylamine **6d** (1.0 g, 3.0 mmol) in 600 mL of ammonia/ammonium buffer solution and subsequent separation by column chromatography (petroleum ether/EtOAc, 98:2), the indole **10d** was recrystallized from petroleum ether/diethyl ether and was obtained as a cream-coloured crystalline product; m.p. 76−77°C; 0.64 g, 71%. − IR (KBr): $\tilde{\nu}$ = 3301, 1492, 1453, 1444, 1329, 1299, 1215, 1124, 1091, 1042, 855, 776, 740, 695, 427 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.57 (dm, *J* = 7 Hz, 1 H, 7-H), 7.53−7.45 (m, 5 H), 7.38−7.21 (m, 7 H), 7.11 (ddd, *J* = 7.8, 7.1, 1.2 Hz, 1 H, 5-H), 7.01 (d, *J* = 3.3 Hz, 1 H, 2-H), 6.24 (dd, *J* = 3.3, 0.9 Hz, 1 H, 3-H), 5.62 (d, *J* = 2.1 Hz, 1 H, CH), 5.32 (d, *J* = 2.1 Hz, 1 H, exch.-D_2O, N−H). − ^{13}C NMR ($CDCl_3$): δ = 141.0, 135.1, 128.6, 128.4, 127.7, 127.5, 126.6, 121.6, 121.1, 119.6, 108.9, 98.9, 68.7. − HRMS (EI, 70 eV); *m/z* (%): 298.1477 (9.5) [M^+], 168 (12.3), 167 (100), 165 (16.1), 152 (7.6), 104 (2), 89 (1.5), 77 (6.6); $C_{21}H_{18}N_2$ requires [M^+] at 298.1469. − $C_{21}H_{18}N_2$: calcd. C 84.53, H 6.08, N 9.38; found C 84.47, H 6.01, N 9.08.

***N*-Phenyl-1-aminoindole** (**10e**): After "redox" electrolysis of 2-(*ortho*-nitrophenyl)-*N*-phenylethylamine **6e** (1.0 g, 4.0 mmol) in 500 mL of ammonia/ammonium buffer solution and subsequent separation by column chromatography (petroleum ether/CH_2Cl_2, 80:20), the indole **10e** was recrystallized from petroleum ether/diethyl ether and was obtained as a white crystalline product; m.p. 84−86°C; 0.51 g, 62%. − IR (KBr): $\tilde{\nu}$ = 3309, 1603, 1495, 1457, 1221, 745, 692 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.78 (m, 1 H, 7-H), 7.38−7.22 (m, 5 H, 6-H, 5-H, 4-H, 3′-H), 7.2 (d, *J* = 3.3 Hz, 1 H, 2-H), 6.97 (t, *J* = 7.5 Hz, 1 H, 4′-H), 6.62 (dd, *J* = 3.3, 0.8 Hz, 1 H, 3-H), 6.52 (d, *J* = 7.7 Hz, 2 H, 2′-H), 6.39 (s, 1 H, exch.-D_2O, N−H). − ^{13}C NMR ($CDCl_3$): δ = 147.2, 135.7, 129.3, 128.6, 126.5, 122.3, 121.0, 120.3, 112.5, 109.4, 100.6. − HRMS (EI, 70 eV); *m/z* (%): 209 (16.1) [M^+ + 1], 208.0999 (100) [M^+], 207 (27.9) [M^+ − 1], 180 (14.5), 131 (9.7), 117 (20.9), 116 (34.4), 92 (28.7), 89 (24.3), 77 (7.3), 65 (30.8), 63 (19.5), 39 (9.5); $C_{14}H_{12}N_2$ requires [M^+] at 208.1000. − $C_{14}H_{12}N_2$: calcd. C 80.74, H 5.81, N 13.45; found C 80.8, H 5.76, N 13.25.

***N*-(*para*-Methoxyphenyl)-1-aminoindole** (**10f**): After "redox" electrolysis of 2-(*ortho*-nitrophenyl)-*N*-(*para*-methoxyphenyl)ethylamine **6f** (0.7 g, 2.5 mmol) in 600 mL of ammonia/ammonium buffer solution and subsequent separation by column chromatography (petroleum ether/EtOAc, 93:7), the indole **10f** was recrystallized from petroleum ether/diethyl ether and was obtained as a white crystalline product; m.p. 114−116°C; 0.38 g, 65%. − IR (KBr): $\tilde{\nu}$ = 3306, 1509, 1452, 1244, 1219, 1032, 823, 748, 721 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.68 (m, 1 H, 7-H), 7.32−7.12 (m, 4 H, 6-H, 5-H, 4-H, 2-H), 6.77 (dm, *J* = 9 Hz, 2 H, 2′-H), 6.55 (dd, *J* = 3.3, 0.7 Hz, 1 H, 3-H), 6.46 (dm, *J* = 9 Hz, 2 H, 3′-H), 6.36 (s, 1 H, exch.-D_2O, N−H), 3.73 (s, 3 H, OCH_3). − ^{13}C NMR ($CDCl_3$): δ = 154.4, 141.0, 135.7, 128.6, 126.5, 122.2, 120.9, 120.2, 114.6, 114.1, 109.4, 100.4, 55.5. − HRMS (EI, 70 eV); *m/z* (%): 238.1115 (20.3) [M^+], 123 (13.5), 122 (100), 117 (10.5), 108 (6.7), 95 (11.7), 89 (11.2), 63 (4.1); $C_{15}H_{14}N_2O$ requires [M^+] at 238.1106. − $C_{15}H_{14}N_2O$: calcd. C 75.61, H 5.92, N 11.76, O 6.71; found C 75.43, H 6.13, N 11.74, O 6.68.

1-Oxy-1,2-di[*ortho*-(anilinoethyl)phenyl]diazene (**13**): After two-step electrolysis (reduction then oxidation) of 2-(*ortho*-nitrophenyl)-*N*-phenylethylamine **6e** (1.0 g, 4.0 mmol) in 150 mL of ammonia/ammonium buffer solution in a mercury electrode batch cell, followed by workup and separation by medium-pressure column chromatography (petroleum ether/ethyl acetate, 85:15), the substituted azoxybenzene **13** was isolated as orange oil; 0.350 g, 35%. − IR (KBr): $\tilde{\nu}$ = 3393, 3010, 2927, 1603, 1508, 1488, 1459, 1433, 1323, 1287, 1262, 1180, 750, 693 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 8.42 (dm, *J* = 7.9 Hz, 1 H), 7.71 (dm, *J* = 7.9 Hz, 1 H), 7.6−6.6 (m, 16 H), 4.05 (br. s, 2 H, exch. D_2O, 2× NH), 3.58 (t, *J* = 6.9 Hz, 2 H, CH_2), 3.45 (t, *J* = 6.9 Hz, 2 H, CH_2), 3.25−3.05 (m, 4 H, 2× CH_2). − ^{13}C NMR ($CDCl_3$): δ = 149.5, 147.7, 147.6, 142.3, 136.1, 132.5, 131.15, 130.4, 130.1, 129.2, 129.1, 127.2, 126.7, 123.6, 121.6, 116.9, 112.51, 112.49, 44.65, 44.3, 31.9, 31.0.

***N*-Acetyl-*N*-benzyl-1-aminoindole** (**14**): *N*-Benzyl-1-aminoindole **10c** (0.188 g, 0.847 mmol) was dissolved in dry THF (10 mL) containing acetyl chloride (0.08 g, 1.0 mmol) and triethylamine (0.094 g, 1.0 mmol). The mixture was heated under reflux for 14 h, and then the THF was removed in vacuo in a rotary evaporator. The residual mixture was extracted four times with 10 mL of 1 N HCl and then with CH_2Cl_2 (30 mL). The organic fraction was washed twice with brine (20 mL), dried with $MgSO_4$, and concentrated in vacuo in a rotary evaporator. The crude residue was purified by medium-pressure column chromatography (petroleum ether/ethyl acetate, 90:10) and **14** was obtained as a cream-coloured crystalline product; m.p. 77−79°C; 0.150 g, 70%. − IR (KBr): $\tilde{\nu}$ = 3064, 3029, 2931, 1688, 1456, 1433, 1406, 1320, 1308, 1247, 764, 744, 703 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 7.6 (dm, *J* = 6.7 Hz, 1 H, 4-H), 7.3−7.03 (m, 8 H, Ph-H, 5-H, 6-H, 7-H), 6.62 (d, *J* = 3.4 Hz, 1 H, 2-H), 6.4 (dd, *J* = 3.4, 0.7 Hz, 1 H, 3-H), 5.45 (d, *J* = 14.2 Hz, 1 H, benzyl-CH_2), 4.48 (d, *J* = 14.2 Hz, 1 H, benzyl-CH_2), 1.78 (s, 3 H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 172.3, 135.8, 134.2, 129.05, 128.25, 127.8, 127.2, 126.1, 122.9, 121.1, 120.7, 108.2, 101.6, 51.3, 19.4. − HRMS (EI, 70 eV); *m/z* (%): 265 (21.1) [M^+ + 1], 264.1259 (100) [M^+], 222 (16.9), 221 (14.3), 173 (14.5), 148 (12.3), 131 (95.5), 117 (22.84), 116 (51.8), 106 (23.5), 104 (16.9), 102 (8), 91 (78.8), 89 (12.82), 77 (18.1), 65 (10.4), 63 (5.8), 43 (29.3); $C_{17}H_{16}N_2O$ requires [M^+] at 264.1262. − $C_{17}H_{16}N_2O$: calcd. C 77.24, H 6.1, N 10.59, O 6.05; found C 77.02, H 6.28, N 10.3, O 6.10.

Table 4. Crystal data for **10f**, X-ray data collection parameters, and refinement results[33−35]

Parameters	**10f**[a]
Formula	$C_{15}H_{14}N_2O$
Mol. mass	238.28
Cryst. syst.	Orthorhombic
Space group	$P2_12_12_1$
a	5.623(10)
b	13.826(2)
c	16.063(2)
α	90
β	90
γ	90
V	1248.8(3)
Z	4
ρ_{calcd} [g.cm^{-3}]	1.267
F(000)	504
μ(Mo-K_α) [$^{-1}$]	0.81
T [K]	293
Crystal size (mm)	0.34 × 0.30 × 0.24
Radiation	Mo-K_α
Max. 2Θ [°]	54°
Scan	ω/2θ = 1
t_{max} (for one measurement) [s]	60
Variance of standards	0.4%
Range of *hkl*	0.60; 0.17; 0.20
Unique reflections measured	1528
N(obs)/*N*(var)	1528/206
Final *R* [$I > 2\sigma(I)$]	0.0433
R (all data)	0.070
Σ*w*	1.117
Max. residual el. density [e. Å^{-3}]	0.236
Diffractometer	CAD 4 Nonius

[a] Further details of the crystal structure investigations are available from the Cambridge Crystallographic Data Centre (CCDC) on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) +44 (0)1223 336033; E-mail: deposit@ccdc.cam.ac.uk], on quoting the depository number 101875.

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