Synthesis, Electrochemistry, and Molluscicidal Activity of Nitroaromatic Compounds: Effects of Substituents and the Role of Redox Potential

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Abstract—Molluscicidal bioassays and electrochemical studies (measurement of first wave reduction potential, Epc1) were performed on several synthetic nitroaromatics, in relation to possible correlation between biological activity, redox potential and structural effects. Five of them presented a significant molluscicidal activity on *Biomphalaria glabrata* ($LD_{50} < 20$ ppm). The Epc1 values ranged from -0.532 to -0.857 V versus Ag/AgCl (0.1 M) (-0.260 to -0.585 V versus NHE), all of them, in the favorable range for reduction in vivo. Data comparison between Epc1 and molluscicidal activity indicates that the presence of the electroactive nitro group is important for the biological activity. Correlation with redox potential, however, was not evident. Structural effects seem to be the most important parameter. Higher activity is noticeable for phenols, including the *para*-nitro azo or hydrazo-containing compounds. No activity was observed for compounds having the benzylic substituent in *meta* position to the nitro group. These results suggest that activity undoubtedly involves more than reduction characteristics and that the possible formation of electrophilic species, after nitro reduction, can play an important role in molluscicidal activity against *B. glabrata*. © 2001 Elsevier Science Ltd. All rights reserved.

Introduction

Schistosomiasis is an endemic parasitic disease, affecting the tropical and subtropical regions of the world, and is second only to malaria in the havoc it causes to the social and economic development of countries located in these areas.[1] It is caused by the presence of the worm *Schistosoma mansoni* in the liver of the affected person, the fresh-water mollusk *Biomphalaria glabrata* acting as intermediate host. This disease is in a growing stage due to poverty and lack of basic sanitation. The reduction of its transmission is crucial. The use of molluscicides in the prophylactic treatment promotes the rupture of the evolutionary cycle of the worm with the destruction of its intermediate host, the snail *B. glabrata*.[1]

The molluscicides currently in use are either synthetical or from natural origin. Several of them possess the nitro group functionality. Since the 1960s, the only compound that has been widely and effectively used as a molluscicide in the control of schistosomiasis is the synthetic compound niclosamide (**23**).[2] Niclosamide can kill *B. glabrata* adults at concentrations as low as 1.5 ppm after 2 h exposure. The mode of action of niclosamide against snails and cestodes has received relatively little attention[3] and is still uncertain.[4] From the available data, it is clear that it exerts most of its effects on respiration and carbohydrate metabolism.[4] The main drawback of the use of niclosamide appears to be that formulations cause high fish mortality at concentrations used to control snails.[4] The high cost of these products, together with their toxic effects to non-target organisms and the risk of potential development of heritable resistance has strongly stimulated the search for new molluscicides.[2]

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Reduction potentials provide information on the feasibility of electron transfer (ET) in vivo. Established relationship between the ease of reduction, represented by Epc, $E_{\frac{1}{2}}$ or Eredox, and biological activities, shows the relevance of electrochemical studies as tools for the comprehension of drug mechanism of action against various diseases, for prediction of biological activities and for the design of potentially active compounds. Absolute correlation is not expected, since other factors as solubility, metabolism, diffusion, adsorption, site binding, cell permeability and stereochemistry undoubtedly play critical roles.[5] Significantly large number of physiologically active substances possess $E_{\frac{1}{2}}$ values greater than about -0.5 V versus normal hydrogen electrode (NHE), in the physiological active range, which can permit electron acceptance from biological donors[6] or they can suffer metabolic changes, furnishing easily reduced derivatives.[7] In the case of antihelmintic compounds, electrochemical data was acquired.[8,9] To our knowledge, no previous work has been hitherto done in relation to molluscicidal activity.

The nitroaromatic compounds are exceptional for their range of activity, the relative lack of resistance, and their interesting chemistry.[10] The main chemical parameter that determines the effectiveness of nitro drugs is the reduction potential of the nitro group.[11] There is good evidence that some electrochemical properties of nitro compounds can be correlated with the pharmacological effects of these compounds.[12] This indicates that part of their activity may derive from the nitro-catalyzed production of superoxide (futile cycle) or is due to the action of their reduced metabolites (bioreductive alkylation).

The most biologically relevant measure of nitro group reduction potential is the thermodynamically reversible addition of the first electron, Epc1 (or $E_{\frac{1}{2}}$). Although the values determined in aqueous solutions by cyclic voltammetry (CV) or polarography are not reversible reactions, and for nitroaromatic compounds may involve the addition of up to four electrons, the first is usually the most difficult.[13] The reductive metabolism, in vivo, is carried out by widely distributed constitutive flavo-enzymes that are able to use nitroaromatics as alternative electron acceptors (flavine dependent reductases, cytochrome P_{450}).[14]

The aim of the present study was to conduct laboratory evaluation of molluscicidal activity of synthetic nitroaromatics on the adult snail of *B. glabrata* and compare the results with measured Epc1. Nineteen nitroaromatics and three other compounds, several of them described for the first time, were tested. The compounds were selected from a series of *para-* and *meta*-substituted nitrocompounds, preliminarily synthesized as possible ligands in a program for preparation of new platinum complexes, similar to *cis*-platin, and others with mixed functionalities. Compounds **5** and **6** could be considered standards. Compounds **15** and **16** were commercially available and similar to yurumin (**24**). A wide structural range of compounds was chosen, due to the present interest of establishing a possible correlation between electrochemical parameters and molluscicidal activity in a hitherto unexplored area.

The redox potentials were obtained in aqueous medium (phosphate buffer, pH 7), by use of cyclic voltammetry, using mercury as the working electrode. Biological and electrochemical data were compared. The question of toxicity is not addressed at the present time.

In the area of molluscicides, to our knowledge there is only one report of electrochemical studies and it refers to the electrochemical determination of niclosamide (**23**), with postulation of a possible reduction mechanism involving the transfer of four electrons.[15]

Results and Discussion

The 22 compounds investigated were divided into four groups, I to IV, to facilitate the discussion (Table 1, columns 1 and 2). Group I (**1–5**) is represented by nitrocompounds *para*-substituted with methyl (**5**), or methyl-substituted groups. One of them has one additional substituent (**4**). Group II (**6–16**) comprises compounds where electron donating groups (-OH, -NH$_2$, -NHNH$_2$, -OCH$_3$, -NHCOR) are directly coupled to the *ortho*- or *para*-nitro-substituted aromatic ring. **15** and **16** are similar in structure to yurumin (**24**), an active molluscicide.[16] They were included in group II, since the azo substituent in those structures can be considered electron donating, due to the influence of the *ortho*-phenolic-OH and to the presence of the highly electron-withdrawing *para*-nitro substituent. Group III (**17–19**) is constituted by *meta*-nitro substituted aromatics. Group IV (**20–22**) has no nitro functionality.
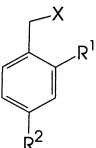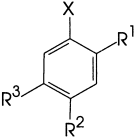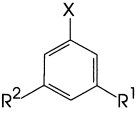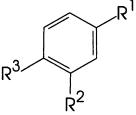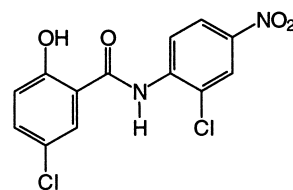

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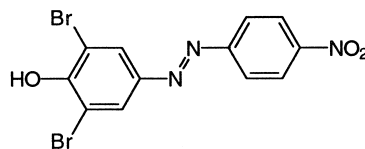
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N-Benzylalkyldiamine or *N*-benzylaminoethanethiol derivatives were easily synthesized, in 60–70% yield, by reacting the respective nitrobenzyl halogenide with the requisite diamine or aminothiol, following a published procedure.[17] The others were obtained from commercial sources.

The biological assay was slightly modified[18] including an inert solvent to allow the complete dissolution of the compounds. This alternative of dissolving the test sample in DMSO with a maximum final solvent concentration of 0.5% v/v[19,20] was tested before, without problems.

Table 1. Analysed substances and their respective groups

Basic structure	Compounds with respective substituents
Group I	**1** X = NH(CH$_2$)$_6$NH$_2$; R^1 = H; R^2 = NO$_2$
	2 X = NH(CH$_2$)$_4$NHCH$_2$C$_6$H$_4$-4-NO$_2$; R^1 = H; R^2 = NO$_2$
	3 X = NH(CH$_2$)$_2$SH; R^1 = H; R^2 = NO$_2$
	4 X = H; R^1 = Cl; R^2 = NO$_2$
	5 X = H; R^1 = R^2 = NO$_2$
Group II	**6** X = OH; R^1 = R^3 = H; R^2 = NO$_2$
	7 X = NH$_2$; R^1 = R$_3$ = H; R^2 = NO$_2$
	8 X = NHNH$_2$; R^1 = R^3 = H; R^2 = NO$_2$
	9 X = NHCOCH$_3$; R^1 = R^3 = H; R^2 = NO$_2$
	10 X = OCH$_3$; R^1 = NH$_2$; R^2 = NO$_2$; R^3 = H
	11 X = NH$_2$; R^1 = NO$_2$; R^2 = OCH$_3$, R^3 = H
	12 X = NH$_2$; R^1 = CF$_3$; R^2 = NO$_2$; R^3 = H
	13 X = NH$_2$; R^1 = H; R^2 = NO$_2$; R^3 = CF$_3$
	14 X = NHNH$_2$; R^1 = H; R^2 = R^3 = NO$_2$

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Group III	**17** X = CH$_2$NH(CH$_2$)$_2$NH$_2$; R^1 = NO$_2$; R^2 = H
	18 X = CH$_2$NH(CH$_2$)$_2$SH; R^1 = NO$_2$; R^2 = H
	19 X = COOH; R^1 = R^2 = NO$_2$

Group IV	**20** R^1 = CF$_3$, R^2 = R^3 = H
	21 R^1 = CF$_3$, R^2 = R^3 = NH$_2$
	22 R^1 = CH$_2$NH(CH$_2$)$_4$CH$_2$C$_6$H$_5$, R^2 = R^3 = H

The potentials of the first waves were obtained, using Ag/AgCl as a reference electrode and calculated in relation to NHE electrode.[21–23] Figure 1 is representative of cyclic voltammograms and the Epc1 value is obtained directly from the curve. Epc1 of compound **16** was measured at pH 9, to help dissolution and **15** was not analyzed by cyclic voltammetry due to its lack of solubility, even at higher pH.

Table 2 lists the values of LD$_{50}$ against *B. glabrata* (column 2), together with the potentials of the first wave for the electrochemically active compounds (columns 3 and 4).

In the biological assays, some compounds presented a significant molluscicidal activity on *B. glabrata* with LD$_{50}$ < 20 ppm, specifically 0.7, 1.8, 6.4, 7.6, and 8.2, for **8**, **4**, **16**, **15**, and **6**, respectively. Some of them were superior to various synthetic or plant molluscicides such as muzigadial, LD$_{50}$ = 5 to 10 ppm; warburganal, LD$_{50}$ = 2 ppm and mukaadial, LD$_{50}$ = 20 ppm,[24] but, still less active than pentachlorophenol, LD$_{50}$ = 0.06 ppm (LD$_{90}$ =
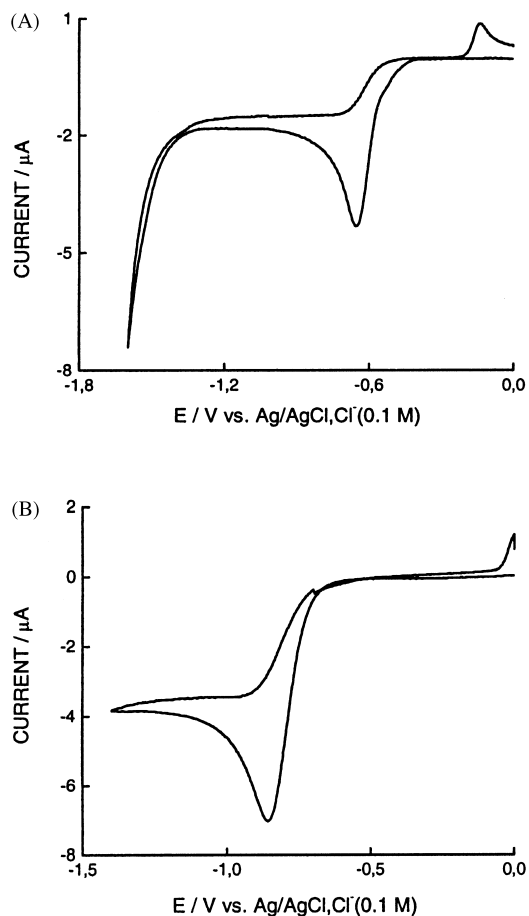
Figure 1. Typical cyclic voltammograms of nitroaromatics, aqueous buffered medium, pH 7.0, Hg electrode, versus Ag/AgCl (0.1 M), 0.035 V s^{-1}: (A) compound **1** (1 mM); (B) compound **6** (1 mM).

Table 2. Biological and electrochemical data of the substances

Substance	LD$_{50}$ (ppm)	Epc1 versus Ag/AgCl	Epc1 versus NHE
1	72.4	−0.532	−0.260
2	40.2	−0.541	−0.269
3	116.5	−0.533	−0.261
4	1.8	−0.606	−0.334
5	100.7	−0.556	−0.284
6	8.2	−0.857	−0.585
7	56.1	−0.840	−0.568
8	0.7	−0.833	−0.561
9	I	−0.773	−0.501
10	I	−0.762	−0.490
11	86.8	−0.730	−0.458
12	55.6	−0.840	−0.568
13	52.9	−0.816	−0.544
14	32.1	−0.743	−0.471
15	7.6	ND	ND
16	6.4	−0.699[a]	−0.427
17	I	−0.636	−0.364
18	I	−0.597	−0.325
19	I	−0.558	−0.286
20	I	—	—
21	I	—	—
22	I	—	—

[a]pH 9.

0.15 ppm)[25] and niclosamide, $LD_{50} = 0.06$ ppm ($LD_{90} = 0.10$ ppm).[25]

The others are reasonably active, with $LD_{50} < 60$ ppm (**2**, **7**, **12**, **13**, and **14**). The compounds were recognized as inactive (**9**, **10**, **17**, **18**, **19**, **20**, **21**, and **22**), or poorly active, when, in preliminary tests, they killed less than 40% of the initial number of snails or, after, at the accurate tests, their LD_{50} were greater than 60 ppm (**1**, **3**, **5**, and **11**).

The Epc1 values ranged from −0.532 to −0.857 V versus Ag/AgCl (0.1 M) (−0.260 V to −0.585 V versus NHE), all of them, in the favorable range[6,7] (versus NHE), to be reduced in vivo. The order of nitro reduction facility, related to their electron affinity, represented as Epc1 is **1** > **3** > **2** > **5** > **19** > **18** > **4** > **17** > **16** > **11** > **14** > **10** > **9** > **13** > **8** > **12** = **7** > **6**. The compounds **20**, **21** and **22** were electroinactive. The range of redox potential for active compounds is very broad and no correlation with molluscicidal activity is evidenced. Data comparison between Epc1 and molluscicidal activity (Table 2, column 2 versus columns 3 or 4), in spite of the relatively small number of some derivatives, suggests that the presence of the nitro group is important for the biological activity, as well as its appropriate location in *ortho-* or *para-* to electron donating groups. No activity was evidenced for compounds of groups III or IV (**17**–**22**). Higher activity is noticeable for phenol derivatives (**6**, **15** and **16**), for mononitrohydrazo derivative (**8**) and for chlorine substituted nitrotoluene (**4**).

A more detailed analysis of the relationship between electroactivity and structural parameters will be reported elsewhere.

These results suggest that the reductive activation may contribute to the molluscicidal activity, but undoubtedly involves more than reduction characteristics. This fact may indicate that the armory of reductases present in the mollusk are able to reduce the nitro group in different environments. As shown in the schistosome area, correlation with redox potential was also not evident.[26]

The possible formation of electrophilic species, after nitro reduction, may play an important role in molluscicidal activity against *B. glabrata* (Fig. 2, pathways A and B). Reduction of the electron-withdrawing nitro group gives the strong electron donating amino or hydroxyamino substituent, which can stabilize an incipient benzyl cation in the transition state of a reaction. Therefore, *ortho-* or *para*-aminobenzyl compounds possessing a good leaving group are very reactive and the benzylic substitution generally occurs by an elimination–addition mechanism involving a very electrophilic quinonimine methide intermediate (Fig. 2A).[27] Additionally, electron-donating groups can originate electrophilic species, by interaction with the electrogenerated hydroxyamino derivative (Fig. 2B).

The activity may be related to the above mentioned facts or other features not yet identified, for example, the nitroso derivatives (2 e⁻ reduction) could also par-
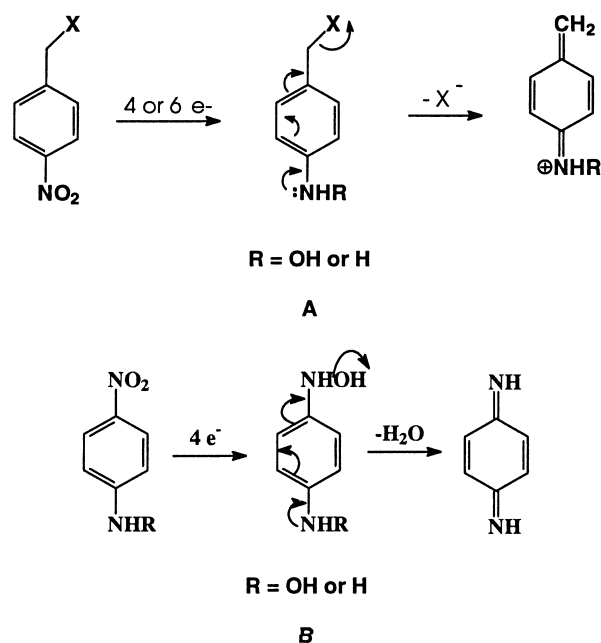

Figure 2. Reductive fragmentation of substituted amino or hydroxy-amino aromatic compounds, generating electrophilic intermediates.

ticipate, as they are, usually, more electrophilic than the parent compounds. It should be also remembered that azonitrocompounds undergo reductive cleavage to amino derivatives.[28] The biological activity in a live host is always a complex outcome not usually dominated by one parameter.

Although nitro-aromatic compounds are probably not the first choice for a drug development, because of their often undesirable side effects, several proved to be suitable for the treatment of tropical diseases.[29]

These results justify the synthesis of derivatives in the most active series and the performance of toxicity tests. Further investigations on the importance of nitro group or azo versus hydrazo groups are under way.

Experimental

Melting points were determined on a MQAPF apparatus and were uncorrected. Infra-red spectra were obtained in KBr on a Bonem FT IR MB-102 spectrometer. NMR spectra were recorded on a Bruker Avance DRX 200 and DRX 400 spectrometers.

Electrochemical measurements

Cyclic voltammetry (CV) was performed using a PAR model 273 A/PAR EG & G potentiostat/galvanostat equipped with an HP 7090A measuring plotter system. A 386 SX/Microtec compatible PC controlled the whole system. A SMDE 303 A/EG & G PARC hanging mercury electrode (area 0.009664 cm^2) was used as the working electrode, together with a platinum counter-electrode and a home-built Ag/AgCl/NaCl (0.1 M) Luggin reference electrode, isolated from the solution by a Vycor® rod. The scan rate was in the range 0.020–35 V s^{-1}.

Epc1 values, in volts (V), were obtained, in Hg electrode, in phosphate buffered aqueous medium, pH 7, versus Ag/AgCl, Cl⁻ (0.1 M) and calculated versus NHE,[21] except in the case of 16, where pH 9 was used. The scan rate used was 0.035 V s⁻¹. Compounds **1**, **2**, **3**, **17**, **18**, and **22** were analyzed as their respective chloridrates.

Bioassays

The method was slightly modified[18] by inclusion of an inert solvent to help in the dissolution of samples. The compounds (as chloridrates) were dissolved first in a small amount of DMSO and added to dechlorinated water, in order to have a solution 0.1% in DMSO. The bioassay involved basically the immersion of the snail *B. glabrata* adult in the mixed aqueous solution of the compound under investigation at appropriate concentrations and followed a described procedure.[18] In order to verify the snails susceptibility, two control sets were used—one with cupric carbonate at 50 ppm (positive control, killed all the snails) and one with dechlorinated water, 0.1% in DMSO (negative control).[30]

The 100 ppm stock solutions of the test compounds were prepared by adding 2.5 mg of the dry compound to 250 mL of dechlorinated water–DMSO for the preliminary test with adult snails. For the accurate one, the same procedure was used and the desired concentrations were obtained by dilution with dechlorinated water at 0.1% DMSO.

Reagents

All chemicals, reagent grade, were used without further purification. The compounds **4**, **6**, **7**, **8**, **10**, **11**, **12**, **13**, **14**, **15**, **16**, **19**, **20**, and **21** were from commercial sources: 2-chloro-4-nitro-toluene (**4**) 97% from Aldrich; 4-nitrophenol (**6**) 95% from Merck, 4-nitroaniline (**7**) 98% from Merck, 4-nitro-phenylhydrazine (**8**) 98% from Riedel De Haen AG, 2-methoxy-5-nitroaniline (**10**) and 4-methoxy-2-nitroaniline (**11**) 98% from Aldrich, 2-amino-5-nitro-benzotrifluoride (**12**), 5-amino-2-nitro-benzotrifluoride (**13**) from Aldrich, 4,4-dinitro-phenylhydrazine (**14**) 98% from Química Fina LTDA, 4-nitro-benzene-azo-alpha-naphthol (**15**) 98% from Carlo Erba, 4-(4-nitro-phenylazo)resorcinol (**16**) from BHD Chemicals Ltd, 3,5-dinitrobenzoic acid (**19**) 99% from Riedel De Haen AG, benzotrifluoride (**20**) from Aldrich, 3,4-diamino-benzotrifluoride (**21**) from Fluorochem Ltd. The compounds 2,4-dinitrotoluene (**5**) and 4-nitro-acetanilide (**9**) were obtained by nitration of toluene and *N*-acetylation of **7**, respectively. The reagents used for synthesis were 1,4-butanediamine 98% (Fluka), benzyl chloride 99% (Riedel De Haen AG), 1,6-hexanediamine 98% (Aldrich), 2-amino-ethanethiol hydrochloride 98% (Aldrich), 4-nitro-benzyl alcohol 99% (Aldrich) and 3-nitro-benzyl bromide 99% (Aldrich).

Synthesis

The compounds **1**, **2**, **3**, **18**, and **22**, reported here for the first time, and **17** described using different preparation procedures,[31] were synthesized by *N*-alkylation of diamines or aminoethanethiol, with benzyl halogenide derivatives, as described (methods A and B). All the compounds were analyzed as their respective chloridrates. The free base, used for mass spectrometry, was obtained by reaction with methanolic NaOH (pH 11), evaporation of the solvent, followed by flash chromatography of the residue in silica gel.

Method A: synthesis of 1, 2, 17, and 22. The corresponding benzyl chloride (20 mmol) was slowly added during 6 h to ethylenediamine (100 mmol), 1,4-butanediamine (40 mmol) or 1,6-hexanediamine (40 mmol) in ethanol (30 mL). The reaction mixture was stirred for 24 h at room temperature. The solvent was removed and the residue was purified on silica gel, using as eluent dichloromethane/methanol (9/1).

[*N*-(4-nitrobenzyl)]-1,6-hexanediamine 1. Analyzed as its chloridrate. Melting point 234–237 °C. ¹H NMR (D₂O) δ 1.32, 1.59 (2m, 8H, CH₂), 3.02 (m, 4H, C*H*₂N), 4.27 (s, 2H, C*H*₂Ph), 7.63 (d, 2H, H₂, H₃ $J_{2-3}=J_{5-6}=8.5$ Hz), 8.20 (d, 2H, $J_{5-6}=8.5$ Hz, H₅, H₆); ¹³C NMR (CDCl₃) δ 25.5, 25.6, 26.9 (CH₂), 39.7 (*C*H₂NH₂), 47.7 (*C*H₂NH), 50.4 (Ph*C*H₂), 124.6; 131.2; 138.4; 148.6 (Ph). IR (KBr) 3339, 3053, 2944, 1562, 1447, 1063, 819, 710 cm⁻¹. HRMS (C₁₃H₂₁N₃O₂) = 251.31.

Di-[*N*,*N*′-(4-nitrobenzyl)]-1,4-butanediamine 2. Analyzed as its chloridrate. Melting point 235–237 °C. ¹H NMR (D₂O) δ 1.76 (m, 4H, CH₂), 3.08 (m, 4H, CH₂N), 4.32 (s, 4H, CH₂Ph), 7.65 (d, 4H, H₂, H₃, $J_{2-3}=J_{5-6}=8.7$ Hz), 8.24 (d, 4H, $J_{5-6}=8.7$ Hz, H₅, H₆); ¹³C NMR (D₂O) δ 22.7 (CH₂), 46.7 (*C*H₂NH), 50.1 (Ph*C*H₂), 124.2, 130.8, 137.8, 148.2 (Ph). IR (KBr) 3419, 3087, 2981, 1525, 1447, 1049, 870, 748 cm⁻¹. HRMS (C₁₉H₂₅N₄O₄) = 373.41.

[*N*-(3-Nitrobenzyl)]-ethylenediamine 17. Analysed as a free base. Melting point 146–147 °C. ¹H NMR (DMSO-*d*₆) δ 2.67 (t, 2H, $J=6.1$ Hz, C*H*₂NH₂), 2.86 (t, 2H, $J=6.1$ Hz, C*H*₂NH), 3.80 (m, 5H, C*H*₂Ph, NH, NH₂), 7.60 (t, 1H, $J_{5-4}=J_{5-6}=8$ Hz, H₅), 7.80 (dl, 1H, H₆), 8.10 (dd, 1H, H₄), 8.23 (sl, 1H, H₂); ¹³C NMR (DMSO-*d*₆) δ 38.5 (*C*H₂NH₂), 45.4 (*C*H₂NH), 51.3 (*C*H₂Ph), 121.7, 122.5, 129.6, 134.60, 134.8, 143.0, 147.8 (Ph). IR (KBr) 3245, 3062, 1625, 1531, 1343, 1123, 988, 799 cm⁻¹.

Di-(*N*,*N*′-benzyl)-1,4-butanediamine 22. Melting point 241–244 °C. ¹H NMR (D₂O) δ 1.71 (m, 4H, (C*H*₂)₂), 3.02 (m, 4H, 2C*H*₂NH), 4.17 (s, 4H, CH₂Ph), 7.43 (sl, 10H, Ph); ¹³C NMR (D₂O) δ 23.1 (*C*H₂*C*H₂), 46.5 (*C*H₂NH), 51.3 (*C*H₂Ph), 129.5, 129.6, 130.0, 130.1, 130.9 (Ph). IR (KBr) cm⁻¹ 3050, 2995, 2937, 2796, 1591, 1443, 1110, 872, 751, 702.

Method B: Synthesis of 3 and 18. 4-Nitro-benzyl chloride (20 mmol) or 3-nitro-benzyl bromide were slowly added during 4 h to 2-aminoethanethiol hydrochloride (40 mmol) and NaHCO₃ (40 mmol) in ethanol (30 mL). The reaction mixture was stirred for 7 days at room temperature, after which, NaOH aqueous solution was added until pH = 10. The solvent was evaporated under reduced

pressure. The obtained residue was purified on silica gel, using as eluent dichloromethane/methanol (9/1).

[*N*-(4-Nitrobenzyl)]-2-aminoethanethiol 3. Oil. ^{1}H NMR (C_5D_5N) δ 3.05 (t, $J = 6.7$ Hz, 2H, CH_2SH), 3.57 (t, 2H, $J = 6.7$ Hz, CH_2NH), 3.96 (s, 2H, CH_2Ph), 7.60 (d, 2H, $J_{2–3} = 8.5$ Hz, H_2, H_3), 8.15 (d, 2H, $J_{5–6} = 8.5$ Hz, H_5, H_6); ^{13}C NMR (C_5D_5N) δ 29.2 (CH_2SH), 34.9 (CH_2NH), 39.2 (CH_2Ph), 129.8, 130.3, 135.0, 147.5 (Ph). IR (KBr) 2897, 2683, 2582, 1600, 1510, 1351, 1245, 1109, 853, 799, 709 cm^{-1}. Anal. calcd for $C_9H_{12}N_2O_2S.2$ HCl: C, 37.90, H, 4.95; N, 9.82. Found: C, 38.20; H, 5.17; N, 9.53.

[*N*-(3-Nitrobenzyl)]-2-aminoethanethiol 18. Oil. ^{1}H NMR (D_2O) δ 2.77 (t, 2H, $J = 6.7$ Hz, CH_2SH), 3.01 (t, 2H, $J = 6.7$ Hz, CH_2NH), 3.89 (s, 2H, CH_2Ph), 7.65 (t, 1H, H_5, $J_{5–4} = J_{5–6} = 8$ Hz), 7.75 (d, 1H, $J_{5–6} = 8$ Hz, H_6), 8.04 (d, 1H, H_4), 8.12 (s, 1H, H_2); ^{13}C NMR ($CDCl_3$) δ 28.1 (CH_2SH), 34.4 (CH_2NH), 38.6 (CH_2Ph), 112.9, 124.1, 130.3, 136.1, 140.4, 148.4 (Ph). IR (KBr) 3065, 3033, 2924, 2872, 2573, 1531, 1450, 1348, 1127, 930, 811, 709 cm^{-1}. Anal. calcd for $C_9H_{12}N_2O_2S.2$ HCl.H_2O: C, 35.65; H, 5.32; N, 9.24. Found: C, 35.45; H, 5.07; N, 9.13.

Acknowledgements

References and Notes

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