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Unusual Reaction of 1,4-Diamino-2-nitrobenzene Derivatives toward Nucleophiles: Catalysis by Sodium Sulphite

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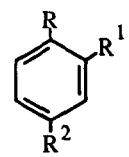
Abstract. Unusual substitution of amino group occurs by reactions of some 1,4-diamino-2-nitrobenzenes (semipermanent hair dyes) and nucleophiles (NH_3, H_2O). The reaction is catalyzed by sodium sulfite. The obtained products are suspected of being toxic substances which may be present in cosmetic matrices. Apparently, this reaction is a nucleophilic aromatic substitution but it may be explained by a mechanism involving a tautomeric form of substrate.

1,4-Diamino-2-nitrobenzene derivatives are semipermanent hair dyes,[1] which are useful in cosmetics. Some of their, and other here considered derivatives, are reported as follows.



	R	R^1	R^2	commercial name
1	$NHCH_2CH_2OH$	NO_2	NH_2	**HCRED 3**
2	NH2	NO_2	NH_2	**NP**
3	$NHCH_2CH_2OH$	NO_2	$NHCH_2CH_2OH$	**HCVIOLET**
4	NH_2	NO_2	$NHCH_2CH_2OH$	**HCRED 7**
5	$NHCH_2CH_2OH$	NO_2	$N(CH_2CH_2OH)_2$	**BLUE SOLID**
6	NH_2,	NO_2	$N(CH_2CH_2OH)_2$	**HCRED 13**
7	$NHCH_2CH_2OH$	NH_2	NO_2	**HCY 5**
8	$NHCH_2CH_2OH$	NO_2	NO_2	
9	$C_5H_{10}N$ (piperidyl)	NO_2	NO_2	
10	SO_3H	NO_2	NO_2	
11	$NH(CH_2)_3CH_3$	NO_2	NO_2	
12	$NHCH_2CH_2OH$	NO_2	H	
13	OH	NO_2	NH_2	
14	OH	NO_2	NO_2	
15	NH_2	NO_2	NO_2	
16	NH_2	NO_2	H	
17	OH	NO_2	$NHCH_2CH_2OH$	
18	OH	NO_2	H	

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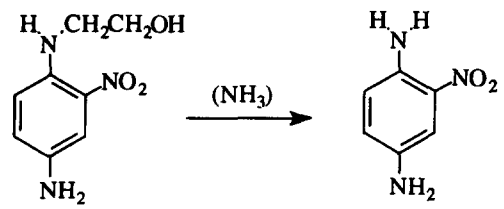
In principle, the stability of hair dyes is important not only for obvious technical requirements, but also because some of their reaction products may be toxic substances. In the XV European Directive (92/86, 21/10/92) a list of forbidden hair dyes is reported because of their potential toxicity.[2]

Recently,[3] in commercial cosmetic samples (which are multicomponent mixtures) containing 1-(N-hydroxyethyl)-2-nitro-1,4-phenylenediamine **1** (**HCRED3**), the presence of 2-nitro-1,4-phenylenediamine **2** (**NP**) was detected. In order to obtain some informations on the origin of **NP**, we investigated this transformation and the possible action of some components of commercial matrix which contains **HCRED3** or other related dyes and the mechanism of formation of **NP**.

Results and discussion

Commercial samples, containing **1** and NH_3, stored at room temperature for several months, show the presence of large amounts of **2**; when they are stored at 70°C for a month, about 50% of **HCRED3** is converted to **2**. This transformation is reported in Scheme 1.



HCRED3 1 **NP 2**

Scheme 1

Apparently, the reaction of Scheme 1 seems to be a nucleophilic aromatic substitution (S_NAr), but it is surprising for two main reasons. The first is that 2-nitro-substituted benzenes (for example 2-nitro-halogenobenzenes) are only moderately activated substrates[4] toward the attack of the nucleophiles and the presence of the amino group in 4 position reduces the activation of the substrate by his strong electron releasing effect. The second reason is that the amino group is a bad leaving group. In particular, primary amino group may be hardly replaced by amines,[5] while instances of replacement of secondary amino groups are reported in literature.[6]

In cosmetic matrix samples, when NH_3 is replaced by hydroxyethylamine, (or by other amines) **HCRED 3** is not converted to **NP** remaining unchanged in commercial samples after 2-3 months at 70°C. This fact is an indication that the formation of **NP** from **HCRED 3** in commercial samples cannot be ascribed to some N-dealkylation reactions of the hydroxy-ethyl group.

After some preliminary experiments on commercial samples and on mixtures of their separate components, we verified the importance of the presence of sodium sulfite which is added as antioxidant in cosmetic matrix. Table 1 reports the main results of the reaction of **HCRED 3** in the presence of NH_3 (or piperidine).

Table 1
Reactions between HCRED3 (1) and ammonia, at 70°C.

Entry	Solvent	Added substances	Time(days)	Yield % 2 (NP)	13
1	H_2O	--	40	40	0
2	DMSO/H_2O[a]	--	40	5	0
3	H_2O[b]	--	40	0	0[c]
4	DMSO/H_2O[a]	Na_2SO_3	1	100	0
5	H_2O	Na_2SO_3	3	80	15
6	H_2O[b]	Na_2SO_3	20	0	80
7	H_2O	Na_2SO_3	5	0	80
8	H_2O	Na_2SO_3(NaOH)	0.2	0	95

a) (10:1 v/v) b) With piperidine. c) **HCRED3** was recovered unchanged from the reaction mixtures.

In aqueous solvents, variable amounts of the corresponding phenol (2-nitro-4-aminophenol) **13** were recovered from the reaction mixtures.

Table 2
Reactions of selected substrates related with nucleophiles in MeOH/H_2O (1:1 v/v) at 70°C.

Entry	Substrate	nucleophiles	time[a]	A (yield %) B (yield %) (see Scheme 2)	
1	**1**	NH_3/Na_2SO_3[b]	3	**2**(80)	**13**(15)
2	**1**	Piperidine/Na_2SO_3[b]	20	**2**(0)	**13**(95)[c]
3	**8**	Piperidine/Na_2SO_3[b]	5	**15**(0)	**14**(90)[c]
4	**1**	NaOH	0.2	**2**(0)	**13**(100)
5	**8**	NH_3	3	**15**(30)	**14**(0)
6	**8**	NH_3/Na_2SO_3[a]	2	**15**(0)	**14**(100)
7	**9**	NH_3	0.5	**15**(100)	**14**(0)
8	**7**	NH_3/Na_2SO_3[a]	20	-----[d]	
9	**5**[e]	NH_3/Na_2SO_3[a]	6	**6**(80)	**14**(0)
10	**10**	NH_3	15m	**15**(100)	**14**(0)
11	**11**	NH_3/Na_2SO_3[b]	12	**15**(30-50)	**14**(30-50)[f]
12	**12**	NH_3/Na_2SO_3[a]	6	**16**(80)	**18**(0)
13	**12**	NH_3	10	------[d]	
14	**3**[g]	NH_3/Na_2SO_3[a]	1	**6**(85)	**17**(10)[h]

a) Days, unless otherwise indicated. b) Substrate/Na_2SO_3 ratio = 1:10. c) No presence of piperidino-substitution products was detected. d) No reactions. e) **BLUE SOLID.** f) Variable and poorly reproducible relative yields. g) **HCVIOLET.** h) No presence of products of substitution of the $N(CH_2CH_2OH)_2$ group was detected.

An interesting fact is offered by entry 4 (Table 1) which clearly indicates that the formation of **NP** in commercial samples easy occurs when the ammonium hydroxide and sodium sulfite (or related derivatives such as sodium hydrosulfite) are present.

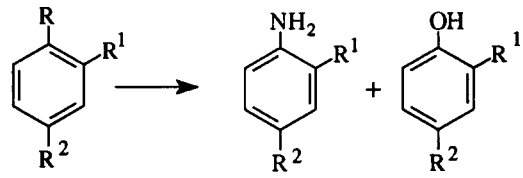
Piperidine is unable to afford substitution products (see entries 2,3 of Table 2): ammonia and water are the only entering groups. The presence of sodium sulfite strongly reduces the times of conversion.

Sulfite ion is known as a powerful nucleophile,[7] and a reasonable intermediate of the reaction of Scheme 1 may be a sulphonate derivative. However, this product was not recovered from the reaction mixtures. Some other data of Table 1 are worthy of consideration.

In S_NAr reactions, piperidine is a better nucleophile than NH_3, but, in the present reaction, the piperidine is unreactive toward **HCRED 3**. (See entry 3). The reaction is depressed by the use of DMSO as solvent (entry 2), while DMSO is well known to favour S_NAr.

The feeble activation of the substrate, the presence of a bad leaving group, the absence of piperidino-substitution product and the negative effect of DMSO are arguments which strongly indicate that the reaction of Scheme 1 cannot occur by the usual two steps mechanism of S_NAr reactions.

Table 2 reports some results obtained for substrates related to **HCRED 3.** Also in this cases the water may compete with ammonia in displacement reactions, as Scheme 2 illustrates.



(A) (B)

Scheme 2

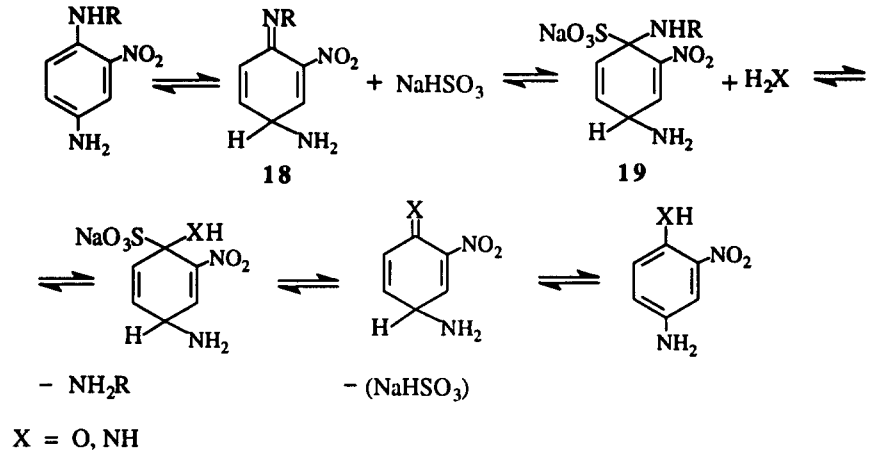
The reactivity of **HCRED 3** may be explained by some possible interactions between the *ortho*-nitro group and the hydroxy group of the amino moiety, to facilitate the leaving group departure. Unfortunately our data cannot be decisive on this possibility. A feeble indication supporting this idea, is that N-butyl-2,4-dinitroaniline **11** reacts with the mixture NH_3/Na_2SO_3 slower (entry 11 of Table 2) than the N-(2-hydroxyethyl)-2,4-dinitroaniline **8** (entry 6 of Table 2). Owing the strong activation of dinitroderivatives, probably these reactions are simple S_NAr reactions.

To have some informations on the behaviour of the hydroxy group of the 2-hydroxy-ethylamine, we detected the rate of the reaction of 2-nitro-fluorobenzene and 2-hydroxy-ethylamine in DMSO (at 25°C) to obtain the aniline derivative **12**. The rate of this reaction (k in s^{-1} mol^{-1} dm^3 = 1.7 x 10^{-3}) is somewhat lower than the value of the similar reactions with 2-nitro-fluorobenzene and 2-N,N-dimethyl-ethylenediamine (k = 3.7 x 10^{-3})[4] and ethylenediamine (3.3 x 10-^{3}).[4] These feeble differences (referred to an S_NAr reaction) cannot be indicative of presence of particular interactions between *ortho*-nitro and hydroxy groups.

The mechanism of reaction of Scheme 1 may be represented by Scheme 3. The first step of Scheme 3 is a tautomeric equilibrium affording the imino compound **18**. The nucleophilic attack of sulfite (or bisulfite) ion on **18** produces the bisulfite adduct **19** which reacts to substitute the NHR group with ammonia or water.

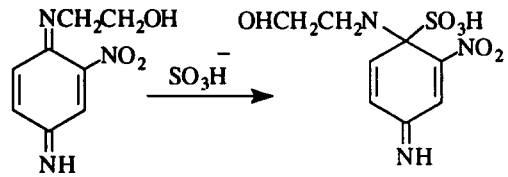
The experimental conditions of reaction of Scheme 1 falls in the field of Bucherer reactions[8] which are well known in naphthalene serie but which are rarely observed in monocyclic derivatives.[9] Even if a pathway of reaction parallel to that of the Bucherer reaction cannot be ruled out, no evidences of the presence of sulphonic group in position 3 of the substrate (as usually accepted by the bucherer mechanism) were obtained.

Other unusual activation of strong electron donor groups (amino and hydroxy groups) toward nucleophilic attack were observed in naphthalene[10] and in 2-thiazoleamine derivatives[11]. In all cases these unexpected reactivities were explained by tautomerism of substrates affording the reactive species.



Scheme 3

The Scheme 3 explains also the reactivity of compound **5** (**BLUE SOLID**) even if it is moderately less reactive than **HCRED 3** (see entry 9). In another mechanicistic hypothesis (depicted in Scheme 4), **21** is an intermediate similar to **19**; **21** should be reached from the quinone imine **20**.



Scheme 4

21-like intermediate cannot be obtained from **BLUE SOLID** and so **21** should explain the decrease of reactivity by passing from **HCRED 3** to **BLUE SOLID**.

Usually compounds **20**-like are obtained by oxidizing reagents which are absent in our reaction mixtures. Consequently, Scheme 4, which is a possible reaction step in permanent dyes use,[12] is a poorly probable reaction path-way to explain reaction of **HCRED 3**.

Probably the presence of the nitro group in position 2 favours the formation of tautomer **18** by acidification of the hydrogen atom of the NHR group and it enhances the attack of nucleophiles on the imino tautomer **18**. In fact, in **HCVIOLET** (**3**) the reaction occurs replacing the $NHCH_2CH_2OH$ group in position 1 (entry 14 of Table 2), while the same group in position 4 is not replaced. Accordingly, **HCY5 7** is unreactive toward the NH_3/Na_2SO_3 mixture (see table 2, entry 8).

The presence of the amino group in 4 position is not completely necessary in activating the substrate. When the amino group in 4 position is absent the reactions with ammonia occurs (entry 12 of Table 2) at lower rate than that of **HCRED 3** (entry 12 of Table 2). In the case of 2-nitro-aniline derivative, the reaction appears to be an S_NAr reaction. However, the importance of sodium sulfite catalysis (entry 13) indicates that

the main reaction pathway may be the mechanism depicted in Scheme 3, even if the possibility of the presence of an S_NAr mechanism with an unusual catalysis by sodium sulfite cannot be completely rouled out. In fact, not only sodium sulfite is well known as powerful nucleophile but also it is a powerful leaving group (see entry 10 of Table 2). However, the behaviour of sulfite as nucleophile needs further investigation. Clearly, the use of sodium sulfite to stabilize the commercial matrix of hair dyes produces a dangerous destabilization of the dyes.

Present data well agree with the pathway of Scheme 3. Probably the nitro group in *ortho* position with respect to the reaction centre, enhance the nucleophilic attack of both, sulfite ion and entering group, while the 4 position is less activated (it is a meta position with respect to the nitro group) and consequently unreactive.

Experimental

General conditions

NMR data were recorded on a Varian Gemini 300 MHz spectrometer. Chemical shifts are reported in ppm relative to solvent ($CDCl_3$ (δ = 7.27), d^6-DMSO (δ = 2.60); d^6-acetone (δ = 2.20); J values are given in Hz. Signals related to N-H and O-H groups disappear after addition of D_2O.
Mass spectra were recorded with a VG-7070E spectrometer.
IR spectra were recorded (in KBr) with a Perkin Elmer mod. 1600 FT-IR spectrophotometer.
UV/VIS spectra were recorded with a Perkin Elmer mod. Lambda 5.
Melting points were determined with a Büchi apparatus and they are uncorrected.
Materials. Amines were commercial samples (Carlo Erba) purified by usual procedures. 1-(N-piperidyl)-2,4-dinitrobenzene **9**,[13] N-butyl-2-4-dinitroaniline **11**[14] were prepared by described procedures. Samples of cosmetic matrix and of separate components (including all the commonly used dyes **1-7**) were obtained from Lowenstein dyes cosmetics, inc. (USA), from Hoechst (Germany) and from S.N.P.E. (France) and used as received. Their structure and purity (>95%) was checked by spectral data which are reported as follows.

1-(N-2-hydroxyethyl)-2-nitro-1,4-phenylenediamine (**HCRED3**) **1** mp 128-130 °C; IR ν_{max}/cm^{-1} 3360, 3340, 3280, 3180, 1560, 1520; ^1H NMR (300MHz, $CDCl_3$): δ 8.05-7.85 (1H, m, NH), 7.53 (1H, d, J=4.6, 3-H), 6.99 (1H, dd, J=8.7, J=2.8, 5-H), 6.82 (1H, d, J=8.8, 6-H), 4.00-3.98 (3H, m, CH_2OH and OH), 3.60-3.40 (4H, m, CH_2NH and NH_2); δ_H in d^6-DMSO 8.05 (1H, t, NH), 7.37 (1H, d, J=2.7, 3-H), 7.14 (1H, dd, J=9.1, J=2.7, 5-H), 7.00 (1H, d, J=9.1, 6-H), 5.06 (1H,t , OH), 5.02 (2H, s, NH_2), 3.80-3.65 (2H, m, CH_2OH),3.50-3.35 (2H, m, CH_2NH); *m/z* 197 (M^+,47), 166 (100), 136 (14), 119 (27).

2-nitro-1,4-phenylenediamine (**NP**) **2** mp 137-140 °C; IR ν_{max}/cm^{-1} 3320, 1590, 1560, 1510 ; ^1H NMR (300MHz, $CDCl_3$): δ 7.44 (1H, d, J = 8.7, J=2.8, 3-H), 6.88 (1H, dd, J=8.8, J=2.8, 6-H), 6.70 (1H, d, J=8.9, 5-H), 5.75 (2H, br s, NH_2), 3.50 (2H, br s, NH_2); δ_H in d^6-DMSO 7.24 (1H, d, J=2.6, 3-H), 7.03-6.90 (4H, m, 5-H, 6-H and NH_2), 4.95 (2H,br s , NH_2); *m/z* 153 (M^+,100), 136 (3), 119 (9), 107 (68).

N,N'-bis(2-hydroxyethyl)-2-nitro-1,4-phenylenediamine(**HCVIOLET**) **3** mp 106-108 °C; IR ν_{max}/cm^{-1} 3330, 1560,1520; ^1H NMR (300MHz, $CDCl_3$): δ 8.10-8.00 (2H, m, NH), 7.87 (2H, dd, J = 8.0, J = 0.6, 7-H), 7.41 (1H,d, J=2.7, 3-H), 7.00 (1H, dd, J=9.3, J=3.0, 5-H), 6.85 (1H, d, J=9.2, 6-H), 4.00-3.85 (4H, m, CH_2OH), 3.55-3.45 (2H, m, CH_2NH), 3.35-3.25 (2H, m,CH_2NH), 1.80-1.60 (2H, br s ,OH); δ_H in d^6-DMSO 8.16 (1H, t, NH), 7.25-7.15 (2H, m, aromatic), 7.05 (1H, d, J=9.1, aromatic), 5.50 (1H, t, NH), 5.05 (1H, t, (OH), 4.83 (1H, t, OH), 3.90-3.65 (4H, m, CH_2), 3.50-3.35 (2H, m, CH2), 3.10-3.00 (2H, m, CH_2); *m/z* 241 (M^+,55), 210 (100) 197 (16), 189 (5).

1-(N-2-hydroxyethyl)-3-nitro-1,4-phenylenediamine (**HCRED7**) **4** mp 100-102 °C; IR ν_{max}/cm^{-1} 3520, 3460, 3350, 1570, 1510; ^1H NMR (300MHz, $CDCl_3$): δ 7.32 (1H, d, J=2.7, 3-H), 6.90 (1H, dd, J=8.9, J=2.8, 5-H), 6.72 (1H, d, J=8.8, 6-H), 5.90-5.70 (2H, br s, NH_2), 4.00-3.85 (3H, m, CH_2OH and NH),

3.40-3.25, (2H, m, CH_2NH), 1.75 (1H, br s, OH); δ_H in d^6-DMSO 7.20-6.90 (5H, m, aromatic and NH_2), 5.40 (1H, t, NH), 4.83 (1H, t, OH), 3.75-3.55 (2H, m, CH_2OH), 3.20-3.05 (2H, m, CH_2NH); *m/z* 197 (M^+,37), 166 (100), 153 (4), 120 (38).

1-(N-2-hydroxyethyl)-N'-(bis-2-hydroxyethyl)-2-nitro-1,4-phenylenediamine **5** (**BLUE SOLID**) mp 82-84 °C; IR ν_{max}/cm^{-1} 3320, 1510; ^1H NMR (300MHz, d6-DMSO): δ 8.05 (1H, t, NH), 7.50-6.95 (3H, m, aromatic), 5.05 (1H, br s, OH), 4.85 (2H, br s, OH), 3.85-3.75, 3.70-3.60, 3.55-3.40, 3.15-3.05 (12 H, m, CH_2); *m/z* 285 (M^+,26), 254 (100), 241 (10), 210 (47).

1-(N-bis-2-hydroxyethyl)-3-nitro-1,4-phenylenediamine (**HCRED13**) **6** mp 91-92 °C; IR ν_{max}/cm^{-1} 3340, 1645,1600, 1530, 1450; ^1H NMR (300MHz, d6-DMSO): δ 8.27 (1H, m, 3-H), 7.90-7.70 (1H, m, 5-H), 7.26 (1H, d, J=9.0, 6-H), 4.50-3.80 (4H, br s, OH and NH_2), 3.70-3.40 (8H, m, CH_2); m/z 241 (M^+,19), 210 (100), 197 (11), 166 (42)

1-(N-2-hydroxyethyl)-4-nitro-1,2-phenylenediamine (**HCY5**) **7** mp 131-133 °C; ^1H NMR (300MHz, d6-DMSO): δ 7.63 (1H, dd, J=8.8, J=2.7, 5-H), 7.53 (1H, d, J=2.7, 3-H), 6.59 (1H, d, J=9.1, 6-H), 6.02 (1H, t, NH), 5.25 (2H, br s, ,NH_2), 4.93 (1H, t,, OH), 3.75-3.65 (2H, m, CH_2OH),3.40-3.30 (2H, m, CH_2NH); *m/z* 197 (M^+,30), 166 (100), 120(38).

N-(2,4-dinitrophenyl)-2-aminoethanol **8.**
0.68 mL (5.38 mmol) of 2,4-dinitrofluorobenzene were dissolved in 4.0 mL of THF/acetone mixture (1/1 v/v). 2.0 mL (10.8 mmol) of ethanolamine were added and the reaction mixture was stirred at room temperature for 60 min. The solvent was removed under vacuum. 1.13 g (yield = 93%) of **8** are obtained after purification by flash chromatography (F.C.) (eluent: ethyl acetate/petroleum light 1/1). mp 89-90 °C (from MeOH); ^1H NMR (300MHz, $CDCl_3$): δ 9.13 (1H, d, J=2.7, 3-H), 8.90-8.70 (1H, m, NH), 8.27 (1H, dd, J=9.6, J=2.6, 5-H), 7.00 (1H, d, J=9.6, 6-H), 4.10-3.90 (2H, m, CH_2OH), 3.70-3.55 (2H, m, $NHCH_2$), 1.94 (1H, br s, OH); *m/z* 227 (M^+, 17), 196 (100), 150 (12), 104(11).

N-(2-nitrophenyl)-2-aminoethanol **12.**
12 was obtained in high yield (98 %) by the same procedures of **8**. DMSO was the solvent of the reaction and the reaction mixture was poured in water, extracted with CH_2Cl_2 and purified by F.C . mp 71-73 °C (from EtOH) ^1H NMR (300MHz, $CDCl_3$): δ 8.35-8.20 (1H, m, NH), 8.20 (1H, d, J=8.9, 3-H), 7.48 (1H, t, 4-H), 6.92 (1H, d,J=8.7, 6-H), 6.70 (1H, t, 5-H), 4.05-3.95 (2H, m, CH_2OH), 3.60-3.50 (3H, m, $NHCH_2$ and OH). *m/z* 182 (M^+, 25), 151 (100), 135 (3), 121 (6), 104 (14), 93 (23).

Reactions between **1** *or related substrates (see tables 1 and 2) and nucleophiles. Typical procedure.*
3.0 mL of aqueous 30% ammonia (or piperidine or aqueous 10% NaOH) and Na_2S0_3 (as indicated in tables 1,2) were added to a solution of 0.050 g (0.25mmol) of **1** in 3.0 mL of solvent (molar ratio substrate:Na_2 $S0_3$ was about 1:10) The reaction mixture was stirred at 70 °C in a sealed vessel. The reaction was monitored by TLC (eluent ethyl acetate/ petroleum light 8/2) The products of the reaction were isolated and purified by F.C. and they were identified by comparison with authentic samples or by spectroscopic analysis.
Physical-chemical data of compounds **9** and **11** are in agreemen with literature.
4-nitro-2-aminophenol **13**; mp 123-125 °C (from EtOH) (lit[15] 125-127 °C) ^1H NMR (300MHz, $CDCl_3$): δ 10.17 (1H, s, OH), 7.36 (1H, m, 3-H), 7.00 (2H, m, 5-H and 6-H), 3.70-3.65 (2H, m, NH_2,); m/z 154 (M^+, 100), 137 (26), 124 (6), 108 (20).

2,4-dinitrophenol **14**; mp 113-115 °C (from acetone) (lit[16] 112-114 °C) ^1H NMR (300MHz, CD_3COCD_3): δ 10.7-10.2 (1H, br s, OH), 9.08 (1H, d, J=2.8, 3-H), 8.67 (1H, dd, J=9.3, J=2.8, 5-H), 7.60 (1H, d, J=9.2, 6-H); *m/z* 184 (M^+,100), 154 (25), 107 (30), 91 (39).

2,4-dinitroaniline **15**; mp 176-178 °C (from EtOH) (lit[17] 176-178 °C); ^1H NMR (300MHz, CD_3COCD_3): 9.09 (1H, d, J=2.7, 3-H), 8.37 (1H, dd, J=9.3, J=2.7,H-5), 8.20-8.00 (2H, br s, NH2), 7.39 (1H, d, J=9.5, 6-H).

2-nitroaniline **16**; mp 70-72 °C, (from H_2O) (lit[18] 73-76 °C); ^1H NMR (300MHz, $CDCl_3$): δ 8.13 (1H, dd, J=8.7, J=1.6, 3-H), 7.37 (1H, m, 4-H), 6.80 (1H, dd, J=1.3, J=8.4, 6-H), 6.72 (1H, m, 5-H), 6.20-5.85 (2H, m, NH_2); *m/z* 138 (M^+, 100), 121 (6), 92 (54).

4-N-(2-hydroxyethyl)-2nitrophenol **17**; mp 112-114°C (from MeOH); ^1H NMR (300MHz, $CDCl_3$): δ 10.23 (1H, s, OH), 7.28 (1H, m, 3-H), 7.01 (2H, m, 5-H and 6-H), 4.12-4.05 (2H, m, CH_2OH and NH), 4.00-3.95 (2H, m, CH_2OH), 3.20-3.15 (2H, m, $NHCH_2$); *m/z* 198 (M^+, 82), 167 (100), 121 (27).

Kinetic data were obtained by usual procedures by u.v./vis spectrophotometric method[4]. The reaction is first order in each reagent. In preparative runs, the only derivative **12** was recovered from the reaction mixtures. No presence of product arising from the attack of the hydroxy group on the 2-nitro-fluorobenzene was detected.

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