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Regioselective and solvent-free arylation of β-nitrostyrenes with mono- and dialkyl anilines

Mohammad A. Ranjbari[1] · Hossein Tavakol[1] · Meghmik Manoukian[1]

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Abstract

A green and solvent-free method were developed for alkylation of N,N-dialkylanilines with substituted β-nitrostyrenes using 10 mol% of choline chloride-zinc chloride deep eutectic solvent at 70 °C. The reaction was highly regioselective and only para-substituted products have been prepared. Despite the sensitivity and weak reactivity of the aniline derivatives for the Friedel–Crafts reaction in acidic media, the presented procedure was successfully carried out this transformation. The synthetic protocol was expanded for the alkylation of pyrrole and indole to produce pharmaceutically active compounds. The reduction of the nitro group of the product to amine was performed using Pd/C and hydrazine to produce amphetamine structure.

Keywords Deep eutectic solvent · Nitrostyrene · Friedel–crafts · Solvent-free · Regioselective

Introduction

The Friedel–Crafts (FC) reaction is an effective standard method to construct the carbon skeleton in aromatic structures [1–5]. The use of catalyst is necessary for this reaction and observing the literature has been revealed that traditional catalysts such as metal oxides and Lewis and Bronsted acids enable to proceed the reaction, in addition to the use of mechanochemistry [6]. However, because of the high cost and the environmental issues of the employed common catalysts, developing new catalysts have been the subject of many studies. Undoubtedly, more efforts need to be paid to provide green conditions for this reaction. Moreover, the FC alkylation of heteroaromatics such as indole and pyrrole have more importance because of

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✉ Hossein Tavakol
h_tavakol@cc.iut.ac.ir

[1] Department of Chemistry, Isfahan University of Technology, Isfahan 84156-83111, Iran

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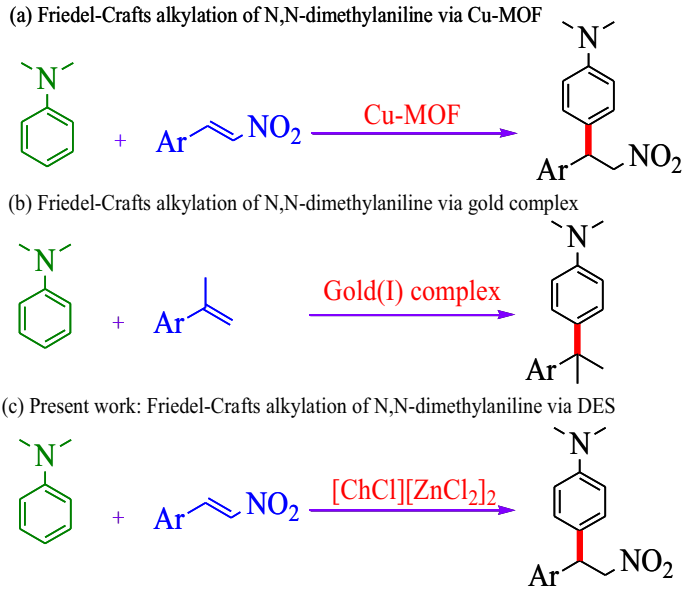
their weak basicity [7]. In addition, the reaction of pyrrole with the β-nitrostyrene is fascinating, and the previous reports use higher temperatures and are less attractive that this work [8, 9]. On the contrary, N,N-dialkylaniline derivatives have some restrictions for this reaction due to their strong basic properties and the possibility of N-alkylation [10, 11]. In this line, the FC alkylation of nitroalkenes has many more benefits, such as providing another functional group for further functionalization and creating the structure of amphetamines (α-methyl ethane amines) after the reduction of the nitro group. Amphetamines are an important class of drugs with intensive effects on the central nervous system (CNS) and useful in the treatment of attention deficit hyperactivity disorder, narcolepsy, and obesity.

By reviewing the literature, only a few reports are available for this type of reaction, which are compared with this work in Scheme 1. For example, alkylation of N,N-dialkylanilines with nitroalkenes compounds using metal–organic framework (MOF, Scheme 1a) [12] and the reaction between N,N-dimethylaniline and alkenes through cyclic-diaminocarbene-gold (I) complex (Scheme 1b) [13].

In addition to the mentioned benefits of this reaction, nitroalkene has been recently employed as an acceptor in Michael-type Friedel–Crafts reaction and because of an easy transformation of nitro into amine, aldehyde, ketone and acid derivatives [14], and synthesis of diverse pharmaceutical compounds, has attracted special attention [15]. As the catalyst of this reaction, conventional Bronsted acid (such as H_2SO_4) or Lewis acid (such as $AlCl_3$, $FeCl_3$, BF_3, and $TiCl_4$) are highly toxic and cause environmental problems [16].

Additionally, reported studies indicated traditional Lewis acid catalysts demand strictly specific conditions, thus are not useful in industry [17]. Since the exploitation



Scheme 1 Friede–Crafts alkylation of N,N-dimethylaniline

of environmental-friendly catalysts has taken over the position of traditional ones in synthetic chemistry, among various green catalysts, significant attention has been focused on ionic liquids because of some distinctive chemical and physical properties such as thermal stability, low vapor pressure, and non-volatility [18, 19]. Deep eutectic solvents (DES) [14] share similar properties with ionic liquids and more importantly, they demonstrate superiority over conventional ionic liquids because of their non-toxicity, biodegradability, and low cost [20, 21]. Furthermore, numerous reports have revealed successful catalytic performance of deep eutectic solvents in Diels–Alder reactions [22], ring opening reactions of epoxides [23], Friedel–Crafts acylation, and Friedel–Crafts alkylation including alkylation of indoles with isatin and homocyclic carbonyl derivatives as well as alkylation of electron enriched arenes with aldehydes [24].

Therefore, after the previous effort on the use of DES in synthetic organic chemistry [25–27], and since solvent-free catalysis has attracted much attention of synthetic chemists from the viewpoint of green chemistry [28–33], it was aimed to successfully perform Friedel–Crafts alkylation of N,N-dialkylaniline derivatives with β-nitrostyrene through low cost and green catalyst (scheme 1c). The reactions have been carried out in solvent-free conditions and only the catalytic amount of choline chloride-zinc chloride (ChCl-$[ZnCl_2]_2$ DES has used with the dual roles of catalyst and solvent.

Results and discussions

In order to assess the optimized reaction conditions, alkylation of N,N-dimethylaniline with β-nitrostyrene has been considered as a model reaction. Different experiments have been designed to optimize the chemical structure and amount of catalyst and the reaction temperature, as the results are listed in Table 1.

The reaction time has been followed by thin-layer chromatography (TLC) to obtain the best time for the completion of the reaction and 6 h was obtained. Then, as mentioned in entries **1–6**, the product was not obtained or obtained in trace amount by the use of water, $FeCl_3$, p-Toluenesulfonic acid, $SnCl_2$, $NiCl_2$, and without a catalyst. However, the desired product was obtained in better yield in $ZnCl_2$ (entry **7**, 30%), but it was not enough. Furthermore, ChCl (entry **8**) and its several DES like ChCl-AcOH (1:1), ChCl-H_2O (1:1), ChCl-Urea (1:2), ChCl-$ZnCl_2$ (1:2), ChCl-$SnCl_2$ (1:2, and ChCl-tartaric acid (1:0.5) were chosen for more screening (entries **9–14**) and only ChCl-$[ZnCl_2]_2$ led to the successful formation of the desired product in 92% yield (entry **14**).

In the next experiments, the ChCl/$ZnCl_2$ molar ratio was changed from 1/2 to 1/3 (this mixture is not DES) and results illustrated a substantial drop in product yield from 92 to 35% (entry **15**).

Comparing the results of entries 7, 8, 14, 15 show that the presence of the DES is necessary for the completion of the reaction and its separated parts of other combination does not lead to the high yield. In the further experiments, the effect of the reaction temperature (entries **16–18**) and the amount of catalyst (entries **19** and **20**)

Table 1 Optimization of the conditions for model reaction

Entry	Catalyst	Time (h)	Temp (°C)	Yield (%)[a]
1	–	6	70	–
2	H_2O	6	70	–
3	$FeCl_3$	6	70	–
4	p-Toluenesulfonic acid	6	70	–
5	$SnCl_2$	6	70	Trace
6	$NiCl_2•6H_2O$	6	70	Trace
7	$ZnCl_2$	6	70	30
8	ChCl	6	70	–
9	ChCl-AcOH	6	70	–
10	ChCl-[H_2O]	6	70	–
11	ChCl-[Tartaric acid]	6	70	–
12	ChCl-[Urea]$_2$	6	70	–
13	ChCl-[$SnCl_2$]$_2$	6	70	20
14	**ChCl-[$ZnCl_2$]$_2$**	**6**	**70**	**92**
15	ChCl-[$ZnCl_2$]$_3$	6	70	35
16	ChCl-[$ZnCl_2$]$_2$	6	90	87
17	ChCl-[$ZnCl_2$]$_2$	6	50	45
18	ChCl-[$ZnCl_2$]$_2$	6	30	–
19	ChCl-[$ZnCl_2$]$_2^b$	6	70	89
20	ChCl-[$ZnCl_2$]$_2^c$	6	70	53

10 mol% catalyst, N,N-dimethylaniline (2.1 mmol), β-nitrostyrene (2 mmol) at 70 °C under argon atmosphere and without the use of solvent

[a]Isolated yields

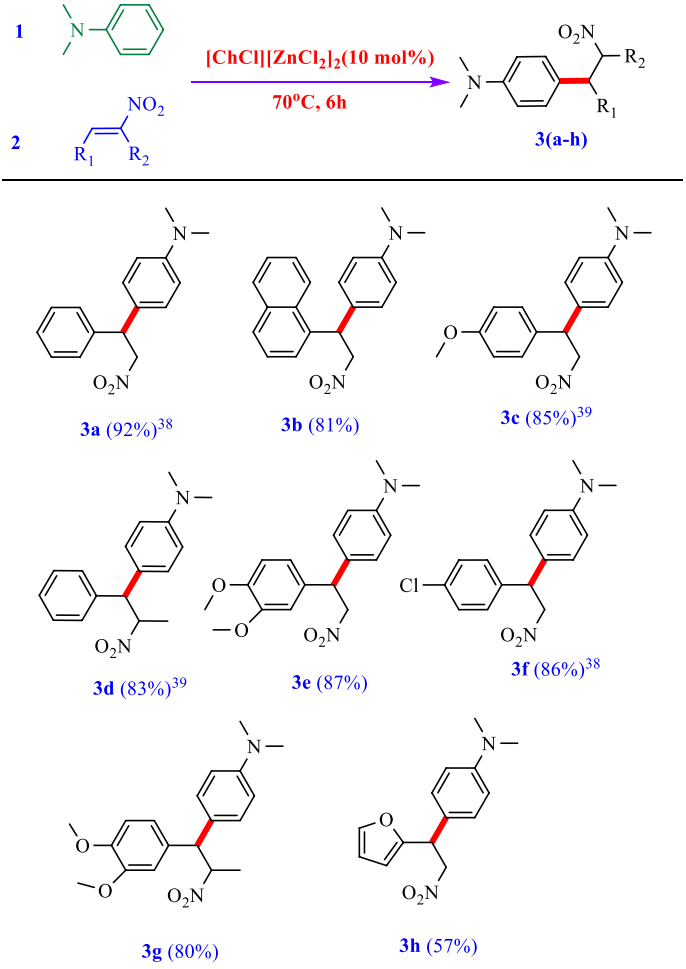
[b]20 mol% ChCl-[ZnCl2]2

[c]5 mol% ChCl-[ZnCl2]2

have been examined, which showed using 10 mol% of catalyst at 70 °C gives the best yield.

After the optimization of the reaction conditions, the versatility of the reaction has been examined by performing the reaction between N,N-dimethylaniline and different β-nitrostyrenes bearing electron-donor and electron-withdrawing substituents under the optimal condition and the results are shown in Scheme 2. To our delight, most of products (**3b**–**3g**) were afforded significant yields (80–87%). However, the alkylation of 2-(2-Nitrovinyl)furan (**3h**) provided a much lower yield (57%), in comparison to previous derivatives.

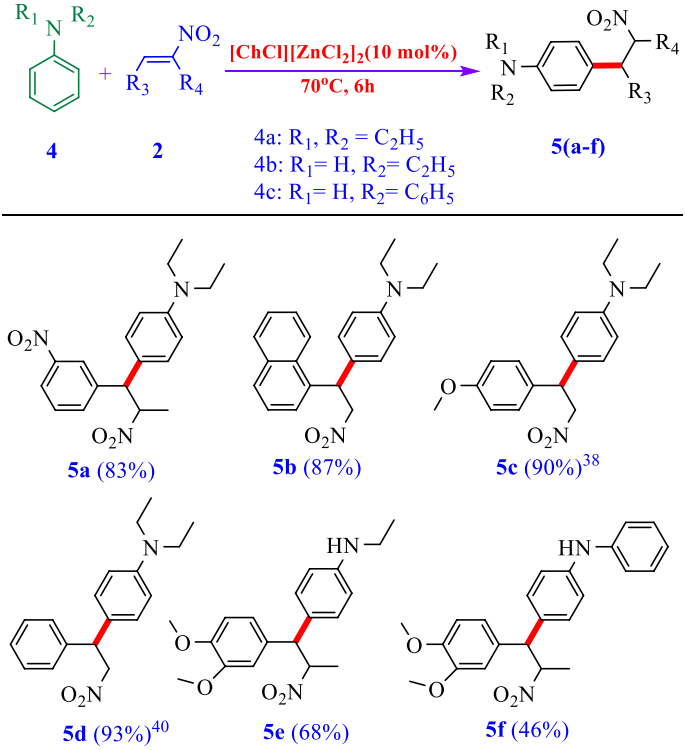
To expand the scope of this reaction and investigate the catalyst's efficiency, different types of N,N-alkyl/arylaniline derivatives, such as N,N-diethylaniline (**4a**), N-ethylaniline (**4b**), and diphenylamine (**4c**), were considered as the other substrates for the arylation of β-nitrostyrenes. As reported in Scheme 3, ChCl-[$ZnCl_2$]$_2$ successfully promoted the production of **5a**, **5b**, **5c,** and **5d** in high yields (83–93%). However, the reactions of N-ethylaniline and N-phenylaniline



Scheme 2 The reaction of various nitroalkanes with N,N-dimethyl anilines catalyzed by EDS. The reference numbers for known compounds were defined with superscript numbers

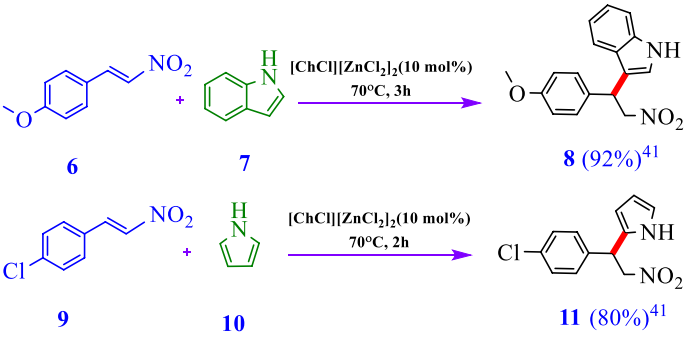
with 1,2-dimethoxy-4-(2-nitro-1-propenyl) benzene gave 68% of **5e** and 46% of **5f**, respectively. The π-electrons delocalization in N-phenylaniline decreases the nucleophilicity and consequently led to product formation in lower yield.

Noticeably, in all of these reactions, only para-alkylated products were afforded and other products such as ortho- or N-alkylation were produced or produced in trace amounts. Based on the literature and according to DFT calculations reported by Ziyaei et al. [34] higher nucleophilicity of para-position in N,N-dialkylanilines is attributed to polar media impact, which pushes electron density toward para-carbon. Since our eutectic solvent played a dual role (catalyst and solvent), it increases the polarity of the reaction media.



Scheme 3 Friedel–Crafts reactions of various nitroalkenes with N,N-dialkylanilines catalyzed by DES. The reference numbers for known compounds were defined with superscript numbers

In order to survey the efficiency of this reaction in more detail, the reaction we explored using of two heteroaromatic rings (structures **7** and **10**) because of the significance of these scaffold in drug discovery and usage of this type of heteroaromatic ring for pharmaceutical purposes [35]. The results, as presented



Scheme 4 Friedel–Crafts alkylation of indole and pyrrole with β-nitrostyrene catalyzed by DES

in Scheme 4, demonstrated that the employed conditions were effectual and expected products were isolated in high yields (product **8** (92%) and **11** (80%)).

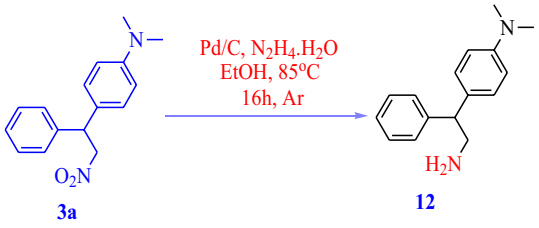
At the final step of this work, the transformation of the nitro group in **3a** into its corresponding amine (to produce **12**) has been examined because of the pharmaceutical importance of the produced amphetamine moiety and since the reported study was shown that this compound has adrenocortical-inhibiting activity [36, 37]. According to Scheme 5, the reduced product was obtained in 95% yield by employing Pd/C as catalyst and hydrazine as a reducing agent in totally two straightforward steps (Friedel–Crafts alkylation and nitro reduction), which are highly promising in comparison with the previous reports on the preparation of this class of compounds.

In summary, mild and green conditions for Friedel–Crafts alkylation of N,N-dialkylanilne with different β-nitrostyrene derivatives have been developed under low cost and non-toxic catalyst system at solvent-free conditions. Sixteen different products were isolated in good to high yields with excellent regioselectivity (only para-substitution) by using 10 mol% of ChCl-$[ZnCl_2]_2$ DES at 70 °C. In this line, the successful alkylation of indole and pyrrole indicated the capability of the employed synthesis. Finally, the reduction of the nitro group of the product to the amine group produces the amphetamine structures, and the sample reaction for a known drug was performed using Pd/C and hydrazine, which produce biologically active products.

Experimental details

Materials and instruments

The employed solvents and other materials have been bought from Sigma-Aldrich, Merck, and Fluka companies in high purities (> 99%, reagent grade). Most of the chemicals have been used without further purification. Melting points were obtained using the Gallen Kamp apparatus. Fourier-transformed infrared (FT-IR) spectra have been recorded using KBr pellets by the Jasco FT-IR instrument. All ^{1}H- and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded using Brucker Ultrashield 300 MHz NMR instrument using $CDCl_3$ or deuterated dimethyl sulfoxide (DMSO-*d6*) as solvents. Elemental analyses were performed using CHNS Vario EL III analyser.



Scheme 5 Reduction of **3a** compound by palladium/C catalyst to their corresponding amine

General Procedure of β-arylation of nitrostyrenes (3a–h and 5a–f; 46–93% isolated yield)

An integrated mixture of eutectic solvent was prepared by the addition of $ZnCl_2$ (2 mmol, 0.272 g) to Choline Chloride (1 mmol, 0.139 g). The mixture was stirred vigorously at 160 °C until the complete dissolution of $ZnCl_2$ salt. Ten mol% (0.082 g) of prepared deep eutectic solvent was added to a brown glass vial. Then, two mmol nitrostyrene and 2.2 mmol N,N-dimethylaniline have been inserted into the mixture. The whole mixture was stirred under the argon atmosphere at 70 °C. The reaction was monitored by TLC, and it was ended after 6 h. Then, distilled water (5 mL) and diethyl ether (2 × 15 mL) were added, and the product has been extracted to the organic layer. After drying (using Na_2SO_4) and removing the solvent of the organic layer, the product was purified using column chromatography on silica gel employing EtOAc:hexane 1:10 (v/v) as eluent.

Synthesis of 3-(1-(4-methoxyphenyl)-2-nitroethyl)-1H-indole (8, 92% isolated yield)

Ten mol% (0.082 g) of prepared deep eutectic solvent was added to a brown glass vial, and two mmol of compound **6** (0.358 g) was added, followed by two mmol of indole (0.234 g) under the argon atmosphere at 70 °C. The termination of the reaction, monitored by TLC, was after 3 h. The product has been extracted to the organic layer using distilled water (5 mL) and ethyl acetate (2 × 15 mL). After drying the organic layer (using Na_2SO_4) and evaporation of the solvent under vacuum, the product was purified using column chromatography (eluting with ethyl acetate: hexane 3:7 (v/v)).

Synthesis of 2-(1-(4-chlorophenyl)-2-nitroethyl)-1H-pyrrole (11, 80% isolated yield)

Ten mol% (0.082 g) of prepared deep eutectic solvent was added to a brown glass vial, and two mmol of compound **9** (0.366 g) was added, followed by three mmol of pyrrole (0.201 g) under the argon atmosphere at 70 °C. The reaction has been followed by TLC, and it has been terminated in 2 h. The extraction of the product was performed using distilled water (5 mL) and two portions of 15 mL ethyl acetate. The organic layer was dried (using Na_2SO_4), the solvent was evaporated (using vacuum), and the product was purified using column chromatography (eluting with ethyl acetate: hexane 3:7 (v/v)).

The Synthesis of 4-(2-amino-1-phenylethyl)-N,N-dimethylaniline (12, 95% isolated yield)

This product has been synthesized using the reported procedure [27]. After the synthesis and removing the catalyst by filtration, its solvent (ethanol) was evaporated under the reduced pressure. The precipitate was washed several times with distilled water, dried over anhydrous Na_2SO_4, and concentrated in vacuum.

The physical and spectroscopic data for prepared structures

The known products were characterized using FT-IR, ^{1}H-NMR, ^{13}C-NMR, and melting points, and their structures were confirmed by comparison of their melting points and spectra with the reports. For unknown products, in addition to the above analyses, elemental analyses were recorded to confirm their structures.

N,N-dimethyl-4-(2-nitro-1-phenylethyl)aniline (3a) yelLow oil (496 mg, 92% yield); FT-IR ν_{maxc}(KBr): 2888, 2828, 1614, 1546, 1525, 1359, 818 cm$^{-1,}$ ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 14.4 Hz, 2H), 7.28 (d, *J* = 6.3 Hz, 3H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 4.98 (dd, *J* = 8.1, 2.5 Hz, 2H), 4.92–4.77 (m, 1H), 2.96 (s, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 149.8, 140.0, 128.9, 128.4, 127.6, 127.3, 126.7, 112.8, 79.6, 48.2, 40.5; Known compound [38].

N,N-dimethyl-4-(1-(naphthalen-1-yl)-2-nitroethyl)aniline (3b) Yellow oil (519 mg, 81% yield); FT-IR ν_{maxc}(KBr): 3419, 2936, 2835, 1614, 1549, 1516, 1267 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 9.1 Hz, 1H), 7.94–7.77 (m, 2H), 7.60–7.35 (m, 4H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.69 (d, *J* = 8.8 Hz, 2H), 5.69 (t, *J* = 8.0 Hz, 1H), 5.22–4.97 (m, 2H), 2.94 (s, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 135.4, 134.2, 131.3, 129.0, 128.6, 128.2, 126.7, 126.3, 125.9, 125.2, 123.9, 123.2, 112.8, 79.4, 43.9, 40.4. Anal. Calcd. (%) for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 72.81; H, 5.59; N, 9.16.

4-(1-(4-methoxyphenyl)-2-nitroethyl)-N,N-dimethylaniline (3c) Yellow oil (510 mg, 85% yield); FT-IR ν_{maxc}(KBr): 3433, 2911, 2803, 1612, 1551, 1511, 1250, 1032, 816 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 8.6 Hz, 2H), 7.11 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 4.95 (d, *J* = 8.9 Hz, 2H), 4.88–4.75 (m, 1H), 3.82 (s, 3H), 2.96 (s, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 158.7, 149.8, 132.1, 128.7, 128.3, 127.0, 114.3, 112.8, 79.9, 55.3, 47.5, 40.5; Known compound [39].

N,N-dimethyl-4-(2-nitro-1-phenylpropyl)aniline (3d) Yellow oil (471 mg, 83% yield); FT-IR ν_{maxc}(KBr): 3433, 2891, 2806, 1613, 1550, 1522, 1355, 800, 698 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.39–7.12 (m, 7H), 6.68 (dd, *J* = 11.6, 8.8 Hz, 2H), 5.47–5.31 (m, 1H), 4.36 (d, *J* = 11.4 Hz, 1H), 2.95 (s, 1H), 2.92 (s, 4H), 2.21 (s, 1H), 1.56 (dd, *J* = 15.6, 6.7 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 149.9,

141.3, 129.2, 128.6, 128.5, 128.4, 127.3, 112.9, 86.5, 55.6, 40.5, 19.5; Known compound [39].

4-(1-(3,4-dimethoxyphenyl)-2-nitroethyl)-N,N-dimethylaniline (3e) Yellow oil (574 mg, 87% yield); FT-IR ν_{maxc}(KBr): 3434, 2930, 1615, 1548, 1515, 1256, 1240, 1140, 1026 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 8.7 Hz, 2H), 6.91–6.64 (m, 5H), 5.01–4.89 (m, 2H), 4.88–4.72 (m, 1H), 3.88 (d, *J* = 3.9 Hz, 6H), 2.96 (s, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 127.7, 123.5, 122.1, 114.6, 108.0, 106.6, 106.5, 75.1, 72.7, 72.3, 71.9, 51.2, 43.1, 35.7. Anal. Calcd. (%) for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 62.66; H, 6.26; N, 8.62.

4-(1-(4-chlorophenyl)-2-nitroethyl)-N,N-dimethylaniline (3f) Yellow oil (524 mg, 86% yield); FT-IR ν_{maxc}(KBr): 2916, 1612, 1551, 1521, 1489, 1352 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 4.95 (d, *J* = 9.4 Hz, 2H), 4.88–4.79 (m, 1H), 2.97 (s, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 150.0, 138.6, 133.2, 129.1, 129.0, 128.3, 126.1, 112.8, 79.4, 47.6, 40.4; Known compound [38].

4-(1-(3,4-dimethoxyphenyl)-2-nitropropyl)-N,N-dimethylaniline (3g) Yellow oil (550 mg, 80% yield); FT-IR ν_{maxc}(KBr): 3416, 2936, 2835, 1614, 1549, 1516, 1267, 1145, 1025 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.30 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.08 (dd, *J* = 14.4, 1.9 Hz, 1H), 6.99 (ddd, *J* = 8.0, 6.1, 1.9 Hz, 1H), 6.86 (t, *J* = 8.7 Hz, 1H), 6.65 (dd, *J* = 12.2, 8.8 Hz, 2H), 5.86–5.70 (m, 1H), 4.27 (dd, *J* = 11.5, 2.4 Hz, 1H), 3.77 (d, *J* = 9.7 Hz, 3H), 3.71 (d, *J* = 5.3 Hz, 3H), 2.85 (s, 3H), 2.83 (s, 3H), 1.42 (dd, *J* = 6.4, 2.5 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.8, 149.8, 149.4, 148.2, 133.7, 129.1, 129.0, 128.4, 128.0, 120.5, 119.7, 113.1, 112.8, 112.5, 112.3, 112.0, 86.7, 86.6, 56.2, 56.1, 55.9, 55.9, 55.2, 55.2, 40.5, 19.5, 19.4. Anal. Calcd. (%) for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 67.68; H, 6.10; N, 8.16.

4-(1-(furan-2-yl)-2-nitroethyl)-N,N-dimethylaniline (3h) Yellow oil (296 mg, 57% yield); FT-IR ν_{maxc}(KBr): 3434, 2889, 2805, 1614, 1555, 1523, 1505, 1375, 1353, 1326, 1165, 741 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 6.33 (s, 1H), 6.13 (d, *J* = 3.2 Hz, 1H), 5.09–4.92 (m, 1H), 4.91–4.71 (m, 2H), 2.98 (s, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 152.9, 150.2, 142.3, 128.6, 124.2, 112.7, 110.4, 107.0, 78.5, 42.8, 40.4. Anal. Calcd. (%) for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 62.75; H, 5.89; N, 11.14.

N,N-diethyl-4-(2-nitro-1-(3-nitrophenyl)propyl)aniline (5a) Yellow oil (592 mg, 83% yield); FT-IR ν_{maxc}(KBr): 3433, 2972, 1612, 1552, 1521, 1351 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 (d, *J* = 10.2 Hz, 1H), 8.17–7.91 (m, 2H), 7.61 (q, *J* = 7.7 Hz, 1H), 7.32 (m, 2H), 6.58 (dd, *J* = 11.5, 8.8 Hz, 2H), 5.94 (m, 1H), 4.64–4.52 (m, 1H), 3.26 (m, 4H), 1.44 (dd, *J* = 13.7, 6.5 Hz, 3H), 1.03 (m, 6H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 148.6, 148.4, 147.1, 147.0, 144.5, 143.7, 135.2, 134.5,

130.7, 130.6, 129.5, 128.8, 126.1, 125.1, 123.4, 122.5, 122.3, 112.2, 111.8, 86.1, 85.9, 54.8, 54.6, 44.0, 43.9, 19.4, 19.2, 12.9, 12.8. Anal. Calcd. (%) $C_{19}H_{23}N_3O_4$: C, 63.85; H, 6.49; N, 11.76. Found: C, 62.92; H, 4.30; N, 12.48.

N,N-diethyl-4-(1-(naphthalen-1-yl)-2-nitroethyl)aniline (5b) Yellow solid (606 mg, 87% yield); mp:129-131; FT-IR ν_{maxc}(KBr): 3434, 2963, 1612, 1556, 1520, 1374, 1197, 783 cm^{-1}; ^1H NMR (300 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.2 Hz, 1H), 7.96–7.76 (m, 2H), 7.62–7.37 (m, 4H), 7.15 (d, *J* = 8.7 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 5.69 (t, *J* = 8.0 Hz, 1H), 5.20–4.99 (m, 2H), 3.34 (q, *J* = 7.1 Hz, 4H), 1.16 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 147.2, 135.5, 134.2, 131.3, 129.0, 128.8, 128.1, 126.6, 125.8, 125.2, 124.9, 123.9, 123.3, 111.9, 79.4, 44.2, 43.9, 12.6. Anal. Calcd. (%) for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 78.23; H, 6.12; N, 8.28.

N,N-diethyl-4-(1-(4-methoxyphenyl)-2-nitroethyl)aniline (5c) Yellow oil (411 mg, 90% yield); FT-IR ν_{maxc}(KBr): 3433, 2970, 2931, 1612, 1552, 1513, 1375, 1251, 1032 cm^{-1}; ^1H NMR (300 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 4.94 (d, *J* = 7.2 Hz, 2H), 4.84–4. 69 (m, 1H), 3.81 (s, 3H), 3.35 (q, *J* = 7.1 Hz, 4H), 1.17 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 158.7, 147.0, 132.1, 128.7, 128.4, 125.8, 114.3, 111.9, 79.9, 55.3, 47.5, 44.3, 12.6; Known compound [38].

N,N-diethyl-4-(2-nitro-1-phenylethyl)aniline (5d) Yellow oil (555 mg, 93% yield); FT-IR ν_{maxc}(KBr): 3434, 2970, 2929, 1613, 1555, 1519, 1356, 1267, 1197, 699 cm^{-1}; ^1H NMR (300 MHz, Chloroform-*d*) δ 7.49–7.19 (m, 5H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 5.12–4.73 (m, 3H), 3.36 (q, *J* = 7.1 Hz, 4H), 1.18 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 147.1, 140.1, 128.9, 128.5, 127.6, 127.3, 125.4, 111.9, 79.7, 48.2, 44.3, 12.6; Known compound [40].

4-(1-(3,4-dimethoxyphenyl)-2-nitroethyl)-N-ethylaniline (5e) Yellow oil (447 mg, 68% yield); FT-IR ν_{maxc}(KBr): 3400, 2965, 1615, 1551, 1516, 1261, 1144, 1024 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.13 (d, *J* = 8.4 Hz, 2H), 7.01 (s, 1H), 6.89 (s, 2H), 6.52 (d, *J* = 8.5 Hz, 2H), 5.47 (s, 1H), 5.34–5.14 (m, 2H), 4.63 (t, *J* = 8.3 Hz, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.2, 148.5, 148.2, 134.0, 128.6, 127.5, 119.9, 112.5, 112.4, 112.1, 79.5, 56.1, 56.0, 48.1, 37.8, 14.9. Anal. Calcd. (%) for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 62.62; H, 4.59; N, 8.20.

4-(1-(4-methoxyphenyl)-2-nitroethyl)-N-phenylaniline (5f) Yellow oil (320 mg, 68% yield); FT-IR ν_{maxc}(KBr): 3396, 3028, 2835, 1597, 1550, 1512, 1314, 1249, 1178, 749 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 8.14 (s, 1H), 7.39–7.30 (m, 2H), 7.29–7.18 (m, 4H), 7.09–7.00 (m, 4H), 6.93–6.86 (m, 2H), 6.81 (d, *J* = 7.3 Hz, 1H), 5.28 (d, *J* = 8.3 Hz, 2H), 4.72 (t, *J* = 8.3 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.7, 143.8, 142.8, 133.1, 132.0, 129.6, 129.2, 128.8, 120.2, 117.3,

117.2, 114.5, 79.4, 55.5, 47.7. Anal. Calcd. (%) for $C_{23}H_{24}N_2O_4$: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.27; H, 5.81; N, 6.96.

3-(1-(4-methoxyphenyl)-2-nitroethyl)-1H-indole (8) Light red solid (545 mg, 92% yield); mp: 148–150; FT-IR ν_{maxc}(KBr): 3379, 2834, 1547, 1511, 1245, 1028, 749 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.04 (s, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.41 (d, J = 2.3 Hz, 1H), 7.39–7.33 (m, 3H), 7.12–7.04 (m, 1H), 7.00–6.90 (m, 1H), 6.90–6.82 (m, 2H), 5.33 (dd, J = 12.9, 8.1 Hz, 1H), 5.25 (dd, J = 12.9, 8.5 Hz, 1H), 5.01 (t, J = 8.2 Hz, 1H), 3.71 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.6, 136.7, 133.1, 129.4, 126.5, 122.6, 121.8, 119.1, 118.9, 114.3, 114.3, 112.0, 79.9, 55.5, 40.5; Known compound [41].

2-(1-(4-chlorophenyl)-2-nitroethyl)-1H-pyrrole (11) Light red solid (400 mg, 80% yield); mp: 102–104; FT-IR ν_{maxc}(KBr): 3433, 2889, 2854, 1613, 1552, 1522, 1490, 1376, 1354, 814 cm^{-1}; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.91 (s, 1H), 7.44–7.32 (m, 2H), 7.25–7.17 (m, 2H), 6.75 (td, J = 2.7, 1.5 Hz, 1H), 6.21 (q, J = 2.8 Hz, 1H), 6.11 (m, 1H), 5.02 (dd, J = 11.6, 6.8 Hz, 1H), 4.96–4.88 (m, 1H), 4.82 (dd, J = 11.6, 7.7 Hz, 1H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 136.6, 134.1, 129.4, 129.3, 128.4, 118.5, 108.8, 106.0, 79.0, 42.4; Known compound [41].

4-(2-amino-1-phenylethyl)-N,N-dimethylaniline (12) White solid (456 mg, 95% yield); mp: 126–128; FT-IR ν_{maxc}(KBr): 3419, 2864, 1616, 1522, 1450, 1164, 699 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.35–7.05 (m, 7H), 6.68 (d, J = 8.6 Hz, 2H), 3.83 (t, J = 7.5 Hz, 1H), 3.12 (d, J = 7.5 Hz, 2H), 3.05 (s, 2H), 2.85 (s, 6H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.5, 144.9, 131.6, 128.8, 128.7, 128.3, 126.3, 113.2, 54.1, 47.2, 40.8; Known compound [41].

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