CHAPTER-3

Denitrosation of Aryl-*N*-Nitrosamines via Trans-Nitrosation Strategy Using Ethanethiol and *p*-Toluenesulfonic Acid under Mild Reaction Conditions

3.1 Introduction

N-Nitrosamines, a class of compounds derived from secondary amines, are studied since the nineteenth century [1]. *N*-Nitrosamines are known as potential carcinogens and mutagenic agents [2]. Nevertheless, *N*-Nitrosamines display various biological properties including anticancer activities (**Figure 3.1A**) [3]. On the other hand, *N*-Nitrosamines are important intermediates in organic synthesis [4]. For example, biologically relevant hydrazines and sydnones are prepared from *N*-Nitrosamines [5]. Recently, *N*-Nitrosamines have been exploited as directing groups for transition metals catalyzed *C*-H activation reactions (**Figure 3.1B**) [6].

While many reactions require *N*-Nitrosamines as starting materials and intermediates, they are also often formed as side products in some reactions. For instance, *N*-Nitrosamine is formed as the major product during the dealkylation process of *N*, *N*-Dialkyl anilines [7].Similarly, *N*-Nitrosamines are formed as the by-product during the preparation of pendimethalin (herbicide) and triazolopyrazine (inhibitor of DPP-4) molecules [8]. Moreover, in many *N*-Nitroso directed *C*-H activation reactions, *N*-Nitroso group remains in the product [6].

In this context, denitrosation of *N*-Nitrosamines plays an important role to regenerate the active amine compound for subsequent applications. However, only a few reports are available for the denitrosation of *N*-Nitrosamines while most of which involve metal-based reducing agents. In particular, CuCl/HCl, [6b, 10], $NiCl_2/NaBH_4$, [6b, 11], $Fe(CO)_5$,[6b, 10],

Raney- Ni/H_2, [6b, 11], Fe/NH_4Cl [6f, 6l] and Zn/NH_4Cl [6j], systems have been used for the denitrosation of *N*-Nitrosamines. Besides the potential toxicity, most of these metal reagents are known for the reduction of other functional groups including nitro, nitrile, aldehyde, ketone, etc. Additionally, some of these methods require excess reagents, strongly acidic or alkaline medium, high temperature, longer reaction time, etc. Therefore, the development of an alternative route is important for process of denitrosation.

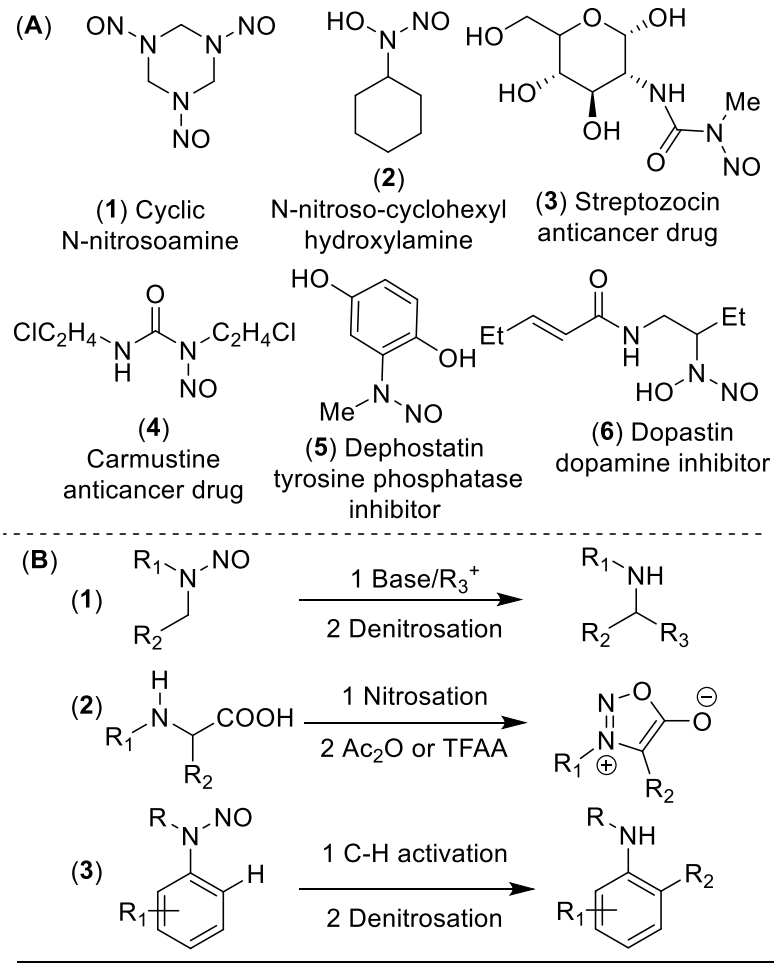
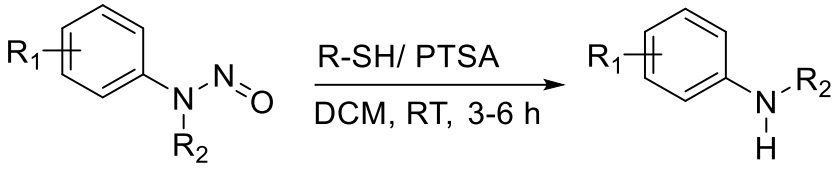


Figure 3.1 A: Biologically relevant *N*-Nitroso compounds. **B:** Applications of *N*-Nitrosamines in some transformations.

Our research group is focused on the chemistry of *N*-Nitrosamines [12] and has reported *N*-Nitrosation of secondary amines using *tert*-butyl nitrite, [12a] reduction of *N*-Nitrosamines to hydrazines, [12b] nitration of aryl amines through *N*-Nitroso intermediate, [12c] activation and *trans*-amidation of secondary amides *via N*-Nitroso intermediate, [12e] etc. Towards this end, recently our group has reported a metal-free method for the denitrosation of aryl *N*-Nitrosamines using iodine-triethylsilane system [12d]. This method was found to be very selective and efficient which tolerates many reactive functional groups during the denitrosation. In continuation of this work, here we developed a new route for the denitrosation of aryl-*N*-Nitrosamines using ethanethiol with PTSA (*p*-Toluenesulfonic acid) *via* trans-nitrosation strategy **(Scheme 3.1**).



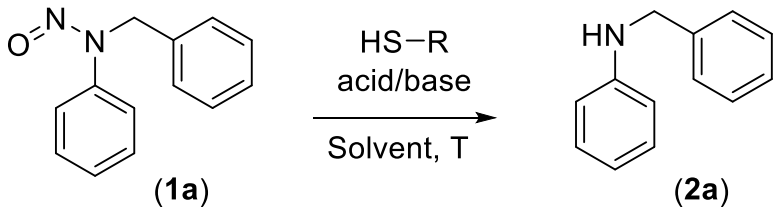
Scheme 3.1 Denitrosation of *N*-Nitrosamines using ethanethiol with PTSA.

3.2 Results and Discussion

At the outset, denitrosation of *N*-Benzyl *N*-Nitroso aniline **1a** was examined with one equivalent of thiophenol in different polar and nonpolar solvents including methanol, acetonitrile, tetrahydrofuran (THF), toluene and dichloromethane (DCM) at 30 °C for 12 h in the absence of any additives (**Table 3.1,** entries **1-5**). Among these solvents, DCM was found to be the best and gave the desired product **2a** in 14% yield. Further, instead of thiophenol, more nucleophilic ethanethiol was used as a nucleophile in DCM at 30 °C for 12 hours.

Under this condition, the yield of the desired product was raised to 21% (**Table 3.1,** entry **6**). Furthermore, the reaction temperature was elevated to 50 °C in order to study the effect of temperature. However, no significant change in the yield was observed (**Table 3.1,** entry **7**). Further, we have increased the amount of ethanethiol from 1.0 equivalent to 3.0 equivalents. The yield of the reaction was increased to 40% with two equivalents of ethanethiol (**Table 3.1,** entry **8**). However, not much change was observed with three equivalents of ethanethiol (**Table 3.1,** entry **9**). Hence, base and acid additives were introduced into the reaction mixture (**Table 3.1,** entries **10-14**). In the presence of a base, no product was observed (**Table 3.1**, entries **10-11**). However, the organic acids such as camphorsulfonic acid (CSA), triflic acid (TfOH) and *p*-Toluenesulfonic acid (PTSA) facilitated the denitrosation process and the desired product **2a** was obtained in good yields in 5 hours (**Table 3.1,** entry **12-14**). Among the different acids, PTSA was found to be better than other acids and gave the desired product **2a** in 89% yield (**Table 3.1,** entry **14**). Moreover, it was also observed that one equivalent of ethanethiol or two equivalents of thiophenol provided the desired product in low yields (**Table 3.1,** entry **15-16**).

Table 3.1 Screening condition for denitrosation[a]



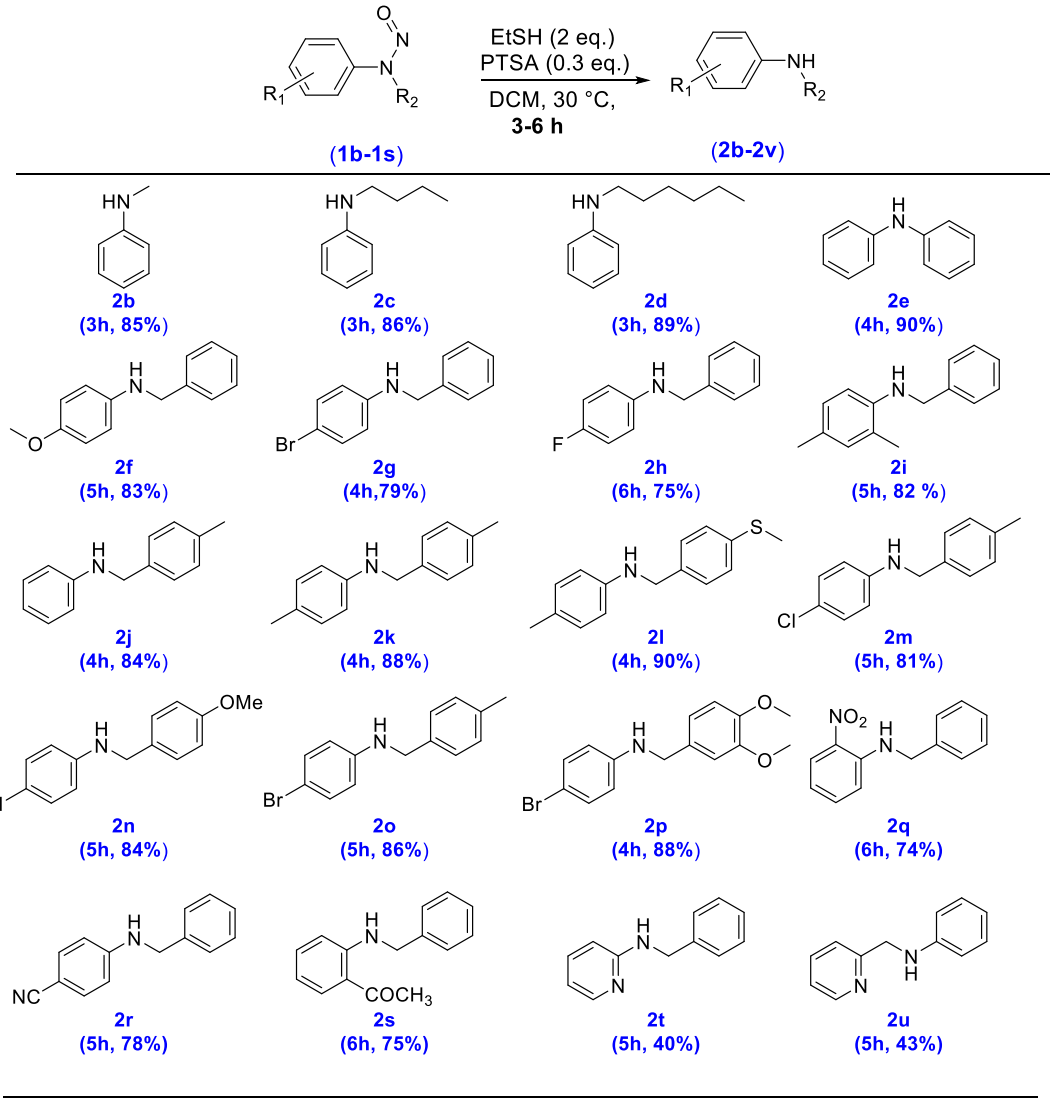
(**1a**) (**2a**)

S.NO	Solvent	Thiol (eq.)	Acid / Base (0.3 eq.)	T (°C)	Time (h)	Yield[b] %
1	CH_3OH	PhSH (1)	-	30	12	Trace
2	CH_3CN	PhSH (1)	-	30	12	~10
3	THF	PhSH (1)	-	30	12	~10
4	Toluene	PhSH (1)	-	30	12	~10
5	DCM	PhSH (1)	-	30	12	14
6	DCM	EtSH (1)	-	30	12	21
7	DCM	EtSH (1)	-	50	12	23
8	DCM	EtSH (2)	-	30	12	40
9	DCM	EtSH (3)	-	30	12	47
10	DCM	EtSH (2)	Et_3N	30	12	~10
11	DCM	EtSH (2)	DBU	30	12	~10
12	DCM	EtSH (2)	CSA	30	5	81
13	DCM	EtSH (2)	TfOH	30	5	84
14	**DCM**	**EtSH (2)**	**PTSA**	**30**	**5**	**89**
15	DCM	EtSH (1)	PTSA	30	5	69
16	DCM	PhSH (2)	PTSA	30	5	75

[a]**Reaction conditions:** N-Nitrosamine (1 mmol), thiol (2.0 eq.), acid/base (0.3 eq.) and solvent (3 ml). [b]Isolated yields.

After finding the optimized reaction conditions, [15] denitrosation of various *N*-nitrosamines was investigated using ethanethiol and PTSA at 30 °C (**Table 3.2**).

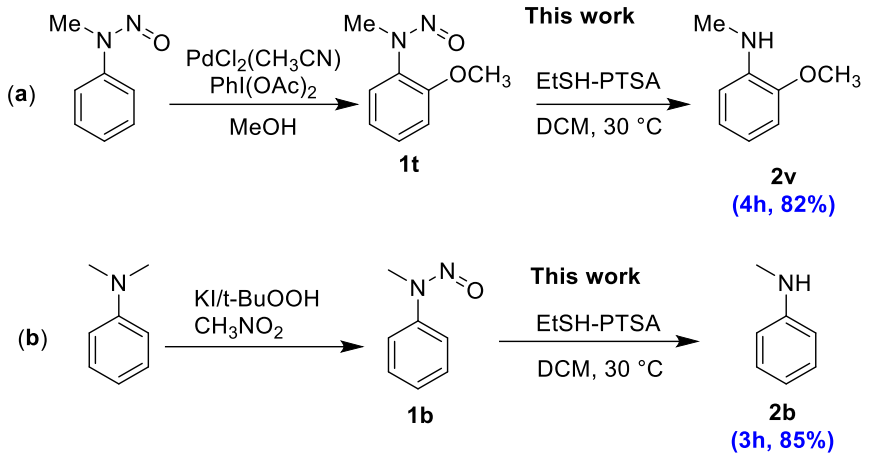
Table 3.2 Denitrosation of *N*-nitrosamines using ethanethiol and PTSA.[a,b]



[a]**Reaction conditions:** *N*-Nitrosamine (1 mmol), ethanethiol (2.0 eq.), PTSA (0.3 eq.) and DCM (3 ml). [b]Isolated yields.

Denitrosation of *N*-Nitroso *N*-Alkyl anilines were achieved in excellent yields (i.e. 85-89%) within 3 hours, irrespective of the length of the alkyl chain present on the substrate (**Table 3.2**, **2b-2d**). Similarly, *N*-Nitroso-*N*-Phenyl aniline gave the desired product **2e** in 90% yield in 4 hours. The substrate scope was further extended by investigating the denitrosation of *N*-Nitroso-*N*-Benzyl anilines. In this series, we have chosen the substrates bearing various electron-donating and electron-withdrawing groups on the aryl rings and were subjected to denitrosation using ethanethiol and PTSA under optimized conditions. To our delight, all these substrates underwent denitrosation and provided corresponding amines in good to excellent yields (**Table 3.2**, **2f-2p**). Moreover, the reduction susceptible functional groups such as nitro, nitrile and ketones were found to be stable during the denitrosation process (**Table 3.2**, **2q-2u**), which increases the scope of the reaction.

After exploring the substrates scope, we investigated the applications of the developed methodology in multistep synthesis **(Scheme 3.2)**. Palladium-catalyzed *N*-Nitrosamine directed *ortho*-alkoxylation of aniline with $PhI(OAc)_2$ in methanol provided the *N*-Nitroso intermediate **1t** in 76% yields [15b]. The compound **1t** was successfully denitrosated to obtain **2v** using EtSH/PTSA in 82% yield (**Scheme 3.2, a**). Similarly, the dealkylation of *N*, *N*-Dimethyl aniline in the presence of KI/*t*-BuOOH in nitromethane provided the *N*-Nitroso intermediate **1b** in 52% yield [15c]. Further, the compound **1b** was subjected to denitrosation using EtSH /PTSA to obtain compound **2b** in 85% yield (**Scheme 3.2, b**).



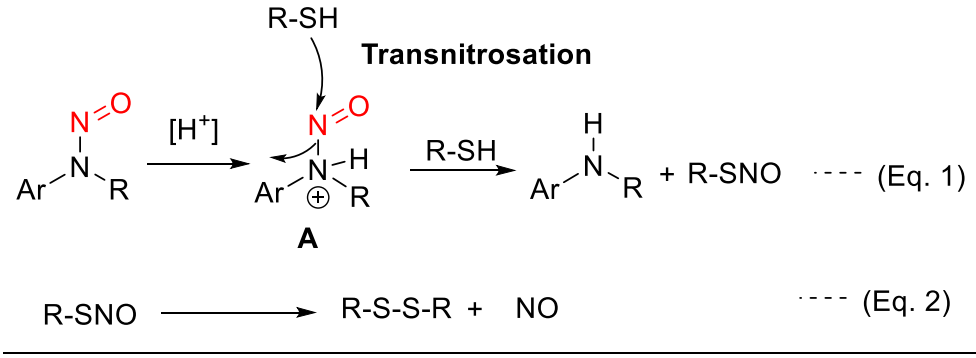
Scheme 3.2 (a) Palladium-catalyzed *C*-H activation followed by denitrosation; (b) Nitrosative dealkylation of *N*, *N*-Dimethylaniline followed by denitrosation.

After exploring the scope of the reactions with *N*-Nitroso arylamines, we investigated the denitrosation of *N*-Nitroso dibenzyl and dialkyl amines under optimized conditions. The denitrosation of *N*-Nitroso dibenzyl amines provided the desired product **2w** only in 7% yield while *N*-Nitroso dihexyl amine failed to undergo denitrosation (**Scheme 3.3**). We believe that alkyl *N*-nitrosamines are more stable when compare with aromatic N-nitrosamines due to some electronic reasons.

Scheme 3.3 Denitrosation of *N*-Nitroso dibenzyl and dialkylamines.

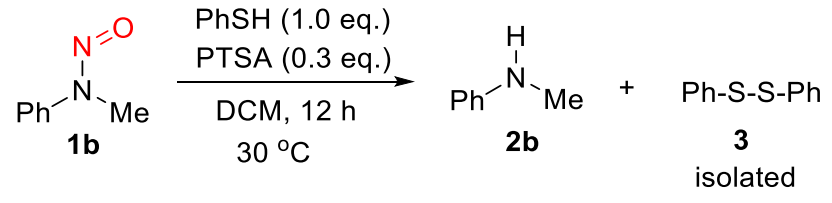
3.3 Proposed mechanism for the reaction

A plausible mechanism for the denitrosation of *N*-Nitrosamines is shown in **Scheme 3.4**. In the first step, *N*-Nitrosamine gets protonated and the intermediate **A** is formed**.** Subsequently, the nucleophile RSH reacts with the intermediate **A** and provides R*S*-NO (via trans-nitrosation) and the amine (**Scheme 3.4,** eq. **1**) [13]. The unstable R*S*-NO converts into disulfide and nitric oxide (**Scheme 3.4**, eq. **2**) [14].



Scheme 3.4 Proposed mechanism for the denitrosation reaction.

To shed light on the proposed mechanism, we have performed a control experiment between thiophenol and *N*-Methyl *N*-Nitroso aniline **1b** in the presence of PTSA (**Scheme 3.5**). In this reaction, the disulfide **3** was isolated in 35% along with the amine **2b**, which supports the proposed reaction mechanism.



Scheme 3.5 Formation of disulfide in the denitrosation reaction.

3.4 Conclusions

In conclusion, we have designed an efficient and useful method for the denitrosation of *N*-Nitrosamines using PTSA and ethanethiol. The reaction proceeds at room temperature and provides the amine in 74–90% yield. Reduction susceptible functionalities such as nitrile, nitro and ketone were found to be stable under the standard reaction conditions. Applications of the current method were demonstrated in multistep organic synthesis. We believe that the current methodology will have a wide scope in organic synthesis.

3.5 Experimental procedures

Procedure for the denitrosation of *N*-Nitrosamines: *N*-Nitrosamine **1a** (1.0 mmol, 1.0 equiv.) was allowed to stir in dichloromethane (3 mL) for 5 min at room temperature to which PTSA (0.3 eq.) and ethanethiol (2.0 eq.) were added. The reaction mixture was further allowed to stir for appropriate time and the progress of the reaction was monitored by TLC. After completion, the reaction mixture was diluted with DCM and washed with water. The organic layer was dried over anhydrous sodium sulphate, concentrated, and subjected to column chromatography (SiO2, eluent: Hexane/ethyl acetate; 92:8) to obtain **2a** as pale-yellow viscous liquid in 89% (164 mg) yield. R_f = 0.62; ^{1}H NMR (500 MHz, CDCl3) δ 7.26–7.19 (m, 4H), 7.18–7.13 (m, 1H), 7.08–7.04 (m, 2H), 6.61 (td, J = 7.4, 1.0 Hz, 1H), 6.50 (dd, J = 8.6, 0.9 Hz, 2H), 4.18 (s, 2H), 3.85 (s, 1H); ^{13}C NMR (125 MHz, CDCl3) δ 148.0, 139.3, 129.1, 128.5, 127.4, 127.1, 117.4, 112.7, 48.1.

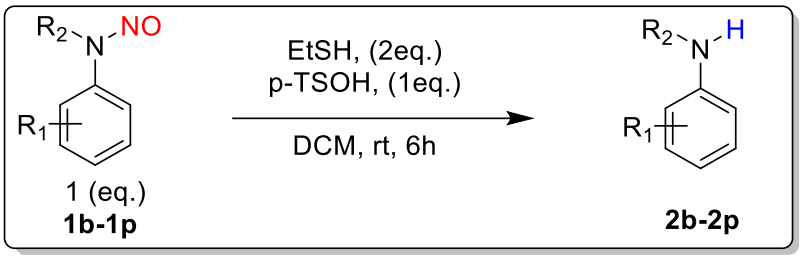
3.5.1 General Experimental procedure for the nitrosation of amines: [12a]

As mentioned in literature, amines (1.0 mmol) and TBN (2 eq.) were taken in dichloromethane solvent and allowed to stir at room temperature for appropriate time. After completion, the reaction mixture was diluted with DCM and washed with water. The organic layer was dried over anhydrous sodium sulphate, concentrated, and subjected to column chromatography (SiO_2, eluent: Hexane/ethyl acetate) to obtain corresponding *N*-nitrosamine products.

3.5.2 General Experimental procedure for the optimization table

N-Benzyl-*N*-Nitrosamine (1 mmol) and thiol (2 eq.) were stirred in the solvent (3ml) at respective time. The acid (0.1 eq.) or base (1 eq.) was used where it is mentioned. The reaction was further allowed to stir for 6 h and the progress of the reaction was monitored by TLC. After completion, the reaction mixture was diluted with dichloromethane and washed with water. The organic layer was dried over anhydrous sodium sulphate, concentrated, and subjected to column chromatography (SiO_2, eluent: Hexane/ethyl acetate) to obtain corresponding pure substituted secondary amines.

3.5.3 General Experimental procedure for the denitrosation of *N*-Nitrosamines



N-Nitrosamine (1.0 mmol, 1.0 equiv.) was allowed to stir in dichloromethane (3 mL) for 5 min at room temperature to which PTSA (1 eq.) and ethane thiol (2 eq.) were added. The reaction mixture was further allowed to stir for 6 h and the progress of the reaction was monitored by TLC. After completion, the reaction mixture was diluted with DCM and washed with water. The organic layer was dried over anhydrous sodium sulphate, concentrated, and subjected to column chromatography (SiO_2, eluent: Hexane/ethyl acetate) to obtain corresponding pure substituted secondary amines.

3.5.4 General Experimental procedure for the preparation of 1t

N-Alkyl- *N*-Nitroso arylamine (1 mmol), $PhI(OAc)_2$ (5mmol) and $Pd(CH_3CN)_2Cl_2$ (0.1 mmol) were charged into a pressure tube containing methanol (4 mL). The mixture was stirred at 30 °C for 24 h. After completion, the mixture was diluted with dichloromethane, washed with water and dried over anhydrous sodium sulphate. The organic layer was concentrated in vacuo and purified in column chromatography.

3.5.5 General Experimental procedure for the preparation of 1b

Tert-Amine (1.0 mmol) and TBAI (73 mg, 0.2 mmol) were placed in a pressure tube to which CH_3NO_2 (4.0 mL) and TBHP (3.0 mmol, 0.4 mL, 70% solution in water) were added. The reaction mixture was stirred at 80 °C for 6 h. After completion, the reaction mixture was quenched with saturated Na_2SO_3 solution and extracted with ethyl acetate. The organic layer was combined and dried with anhydrous Na_2SO_4. Removal of solvent followed by column chromatography using a mixture of hexane and ethyl acetate afforded the desired products.

3.6 Analytical data for denitrosation products

3.6.1. *N*-Benzylaniline (2a): [12d]

The title compound was obtained as pale yellow viscous. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.62; Yield: 88% (167 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26–7.19 (m, 4H), 7.18–7.13 (m, 1H), 7.08–7.04 (m, 2H), 6.61 (td, *J* = 7.4, 1.0 Hz, 1H), 6.50 (dd, *J* = 8.6, 0.9 Hz, 2H), 4.18 (s, 2H), 3.85 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.0, 139.3, 129.1, 128.5, 127.4, 127.1, 117.4, 112.7, 48.1.

3.6.2. *N*-Methylaniline (2b): [15a]

The title compound was obtained as a yellow viscous liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.55; Yield: 85% (97 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37–7.30 (m, 2H), 6.85 (td, *J* = 7.3, 1.0 Hz, 1H), 6.73 (dd, *J* = 8.6, 1.0 Hz, 2H), 3.64 (s, 1H), 2.92 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.2, 129.0, 117.0, 112.2, 30.5.

3.6.3. *N*-Butylaniline (2c): [12d]

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.54; Yield: 86% (132 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.12–7.06 (m, 2H), 6.63–6.57 (m, 1H), 6.53–6.49 (m, 2H), 3.26 (s, 1H), 3.03–3.00 (m, 2H), 1.51 (ddd, *J* = 12.6, 8.4, 6.4 Hz, 2H), 1.35 (dt, *J* = 15.0, 7.3 Hz, 2H), 0.87 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.4, 129.1, 117.0, 112.6, 43.6, 31.6, 20.2, 13.8.

3.6.4. *N*-Hexylaniline (2d): [12d]

The title compound was obtained as a pale yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.58; Yield: 89% (153 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.15–7.04 (m, 2H), 6.61 (ddd, *J* = 7.3, 4.2, 1.0 Hz, 1H), 6.57–6.44 (m, 2H), 3.04–3.00 (m, 2H), 1.54 (dt, *J* = 14.7, 7.3 Hz, 2H), 1.32–1.18 (m, 6H), 0.83 (dd, *J* = 9.5, 4.6 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.4, 129.1, 117.1, 112.7, 44.0, 31.6, 29.5, 26.8, 22.6, 14.0.

3.6.5. Diphenylamine (2e): [16]

The title compound was obtained as a yellow solid. m.p. 56 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.65; Yield: 90% (161 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27–7.19 (m, 4H), 7.09–7.03 (m, 4H), 6.96–6.89 (m, 2H), 5.66 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.0, 129.2, 120.9, 117.7.

3.6.6. *N*-Benzyl-4-methoxyaniline (2f): [17]

The title compound was obtained as a pale yellow solid. M.p. 54 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.60; Yield: 83% (182 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31–7.16 (m, 5H), 6.69 (d, *J* = 8.9 Hz, 2H), 6.51 (d, *J* = 8.9 Hz, 2H), 4.19 (s, 2H), 3.64 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.1, 142.3, 139.6, 128.5, 127.5, 127.1, 114.8, 114.0, 55.7, 49.2.

3.6.7. *N*-Benzyl-4-bromoaniline (2g): [18]

The title compound was obtained as a yellow solid. M.p. 50 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.51; Yield: 79% (213 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 4.7 Hz, 3H), 7.23–7.18 (m, 1H), 7.16 (d, *J* = 2.3 Hz, 2H), 7.15 (d, *J* = 2.1 Hz, 1H), 6.43–6.40 (m, 2H), 4.21 (s, 2H), 4.00 (s, 1H).; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.0, 138.8, 131.8, 128.6, 127.3, 127.3, 114.3, 109.0, 48.19.

3.6.8. *N*-Benzyl-4-fluoroaniline (2h): [19]

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.59; Yield: 75% (160 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44–7.38 (m, 4H), 7.33 (ddd, *J* = 8.6, 5.2, 2.4 Hz, 1H), 6.98–6.88 (m, 2H), 6.63–6.57 (m, 2H), 4.33 (s, 2H), 3.96 (s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.7, 154.9, 144.4, 144.4, 139.1, 128.6, 127.4, 127.2, 115.7, 115.5, 113.6, 113.5, 48.8.

3.6.9. *N*-Benzyl-2,4-dimethylaniline (2i): [12d]

The title compound was obtained as a pale yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.57; Yield: 82% (180 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40–7.16 (m, 5H), 6.88–6.75 (m, 2H), 6.44 (d, *J* = 8.2 Hz, 1H), 4.26 (s, 2H), 3.63 (s, 1H), 2.14 (s, 3H), 2.06 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.7, 139.6, 130.9, 128.5, 127.4, 127.3, 127.1, 126.2, 122.0, 110.1, 48.5, 20.3, 17.4.

3.6.10. *N*-(4-Methylbenzyl)aniline (2j): [20]

The title compound was obtained as a yellow solid. M.p. 45 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.60; Yield: 84% (175 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 7.9 Hz, 2H), 7.10–7.04 (m, 4H), 6.61 (dd, *J* = 10.6, 4.1 Hz, 1H), 6.57–6.49 (m, 2H), 4.17 (s, 2H), 3.86 (s, 1H), 2.25 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.1, 136.7, 136.3, 129.2, 129.1, 127.4, 117.4, 112.7, 48.0, 21.0.

3.6.11. 4-Methyl-*N*-(4-methylbenzyl)aniline (2k): [21]

The title compound was obtained as a pale yellow solid. M.p. 54 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.63; Yield: 88% (193 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.18–7.14 (m, 2H), 7.05 (d, *J* = 6.9 Hz, 2H), 6.92–6.88 (m, 2H), 6.47 (dd, *J* = 8.3, 1.7 Hz, 2H), 4.16 (s, 2H), 3.74 (s, 1H), 2.25 (s, 3H), 2.15 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.9, 136.7, 136.5, 129.6, 129.2, 127.4, 126.6, 112.9, 48.3, 21.0, 20.3.

3.6.12. 4-Methyl-*N*-(4-(methylthio) benzyl)aniline (2l): [12d]

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.61; Yield: 90% (232 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.3 Hz, 2H), 7.15 (dd, *J* = 6.4, 4.4 Hz, 2H), 6.96–6.81 (m, 2H), 6.52–6.40 (m, 2H), 4.18 (s, 2H), 3.80 (s, 1H), 2.39 (s, 3H), 2.15 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.7, 136.9, 136.6, 129.7, 127.9, 126.9, 126.7, 112.9, 48.1, 20.3, 16.0.

3.6.13. 4-Chloro-*N*-(4-methylbenzyl) aniline (2m): [21]

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.61; Yield: 81% (194 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.04–7.00 (m, 2H), 6.46 (d, *J* = 8.9 Hz, 2H), 4.17 (s, 2H), 3.96 (s, 1H), 2.27 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.6, 137.0, 135.8, 129.3, 129.0, 127.4, 122.0, 113.8, 48.0, 21.0.

3.6.14. 4-Chloro-*N*-(4-methoxybenzyl) aniline (2n): [22]

The title compound was obtained as a yellow solid. M.p. 83 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.61; Yield: 84% (218 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.6 Hz, 2H), 8.02 (d, *J* = 8.9 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 5.13 (s, 2H), 4.90 (s, 1H), 4.71 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.8, 146.6, 130.8, 129.0, 128.6, 121.97, 114.0, 113.8, 55.2, 47.7.

3.6.15. 4-Bromo-*N*-(4-methylbenzyl) aniline (2o): [23]

The title compound was obtained as a yellow solid. m.p. 77 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 97:3, R_f = 0.63; Yield: 86% (238 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.16 – 7.13 (m, 4H), 7.06 (d, *J* = 7.7 Hz, 2H), 6.40 (d, *J* = 8.7 Hz, 2H), 4.15 (s, 2H), 3.94 (s, 1H), 2.26 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.0, 137.0, 135.7, 131.8, 129.3, 127.3, 114.3, 108.9, 47.9, 21.0.

3.6.16. 4-Bromo-*N*-(3,4-dimethoxybenzyl) aniline (2p): [12d]

The title compound was obtained as a pale yellow solid. M.p. 106 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.48; Yield: 88% (283 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.18–7.14 (m, 2H), 6.81 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.45–6.41 (m, 2H), 4.14 (s, 2H), 3.79 (d, *J* = 4.0 Hz, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.1, 148.3, 147.0, 131.8, 131.3, 119.5, 114.4, 111.2, 110.6, 109.1, 55.9, 55.8, 48.1.

3.6.17. *N*-Benzyl-2-nitroaniline (2q): [24]

The title compound was obtained as a dark yellow solid. m.p. 75 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.42; Yield: 74% (177 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.11 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.32–7.25 (m, 5H), 7.22 (ddd, *J* = 8.5, 5.2, 2.2 Hz, 1H), 6.73 (dd, *J* = 8.6, 0.8 Hz, 1H), 6.58 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 4.47 (d, *J* = 5.6 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.2, 137.3, 136.1, 132.2, 128.8, 127.6, 127.0, 126.8, 115.6, 114.1, 47.0.

3.6.18. 4-(Benzylamino) benzonitrile (2r): [25]

The title compound was obtained as a yellow solid. m.p. 74 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.62; Yield: 78% (171 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.32 (s, 1H), 7.31–7.28 (m, 1H), 7.28–7.26 (m, 2H), 7.25–7.21 (m, 2H), 6.53–6.50 (m, 2H), 4.57 (s, 1H), 4.30 (d, *J* = 5.3 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.0, 137.7, 133.6, 128.8, 127.6, 127.2, 120.3, 112.3, 99.0, 47.4.

3.6.19. 1-(2-(Benzylamino)phenyl)ethan-1-one (2s): [12d]

The title compound was obtained as a yellow solid. m.p.77 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.46; Yield: 75% (179 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 7.81 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.39–7.28 (m, 6H), 6.69 (d, *J* = 8.5 Hz, 1H), 6.64 (t, *J* = 7.5 Hz, 1H), 4.50 (d, *J* = 5.6 Hz, 2H), 2.64 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.9, 150.8, 138.6, 134.97, 132.6, 128.6, 127.0, 126.9, 117.7, 114.3, 112.1, 46.6, 27.9.

3.6.20 *N*-Benzylpyridin-2-amine (2t): [29]

The title compound was obtained as white solid. m.p. 92 °C. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 85:15, R_f = 0.56; Yield: 40% (76 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.31 – 7.22 (m, 5H), 7.20 – 7.17 (m, 1H), 6.49 (m, *J* = 7.1, 5.1, 0.8 Hz, 1H), 6.27 (d, *J* = 8.4 Hz, 1H), 4.98 (s,

1H), 4.41 (d, *J* = 5.3 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.61, 148.09, 139.13, 137.42, 128.56, 127.33, 127.15, 113.04, 106.70, 46.25.

3.6.21 *N*-(pyridin-2-ylmethyl) aniline (2u): [**29**]

The title compound was obtained as yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 80:20, R_f = 0.49; Yield: 43% (81.7 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.5 Hz, 1H), 7.52 (td, *J* = 7.7, 1.7 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.08 (dt, *J* = 11.7, 5.9 Hz, 3H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 2H), 4.36 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.48, 149.06, 147.80, 136.58, 129.15, 122.00, 121.51, 117.49, 112.96, 49.17.

3.6.22. 2-Methoxy-*N*-Methylaniline (2v): [26]

The title compound was obtained as a yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.51; Yield: 82% (118 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.82 (td, *J* = 7.6, 1.4 Hz, 1H), 6.68 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.59 (td, *J* = 7.7, 1.5 Hz, 1H), 6.52 (dd, *J* = 7.8, 1.4 Hz, 1H), 4.28–4.07 (m, 1H), 3.75 (s, 3H), 2.77 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.8, 139.3, 121.2, 116.2, 109.2, 109.1, 55.3, 30.2.

3.6.23. Dibenzylamine (2w): [27]

The title compound was obtained as a pale yellow liquid. The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 85:15, R_f = 0.52; Yield: 7% (14

mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26–7.22 (m, 4H), 7.19–7.14 (m, 4H), 3.72 (s, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 140.2, 128.3, 128.1, 126.9, 53.0.

3.6.24. 1, 2-Diphenyldisulfane (3): [28]

The title compound was obtained as a white solid. m.p.63 °C The residue was purified by column chromatography in silica gel eluting with hexane:EtOAc 92:8, R_f = 0.61; Yield: 79% (118 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (t, *J* = 1.6 Hz, 2H), 7.54–7.53 (m, 2H), 7.36–7.34 (m, 2H), 7.34–7.32 (m, 2H), 7.29–7.28 (m, 1H), 7.26 (d, *J* = 5.4 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 136.9, 129.0, 127.4, 127.1.

3.6 Spectra of Few Compounds

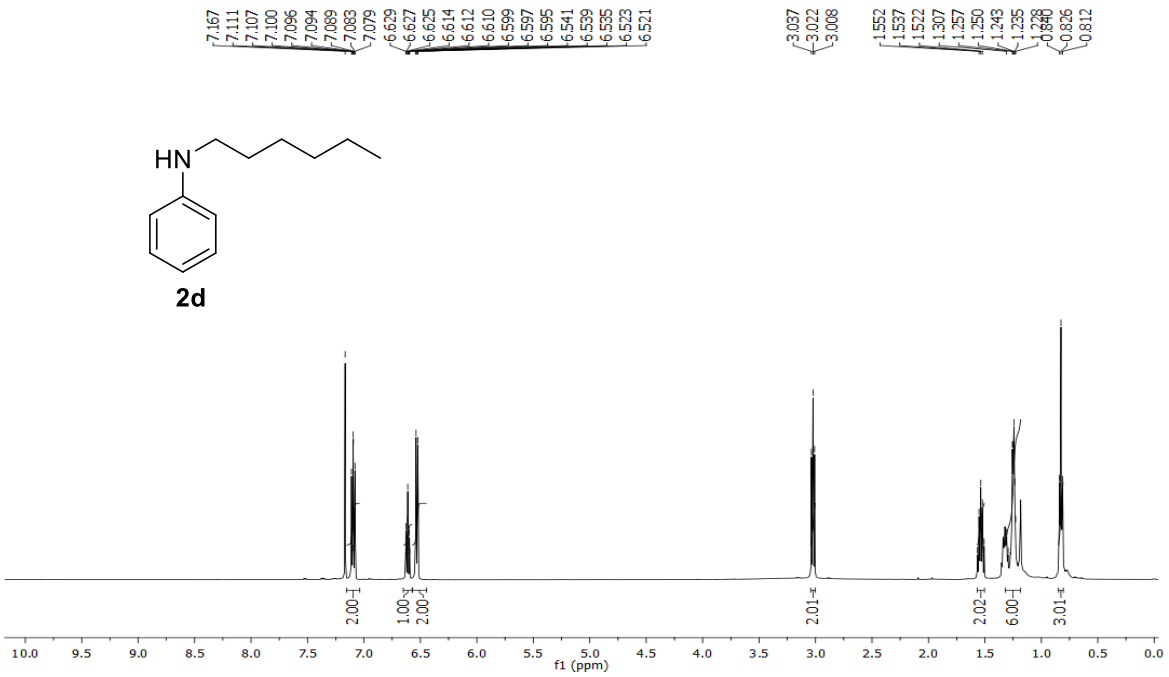


Figure 3.2. ^{1}H NMR Spectra of product 2d in $CDCl_3$

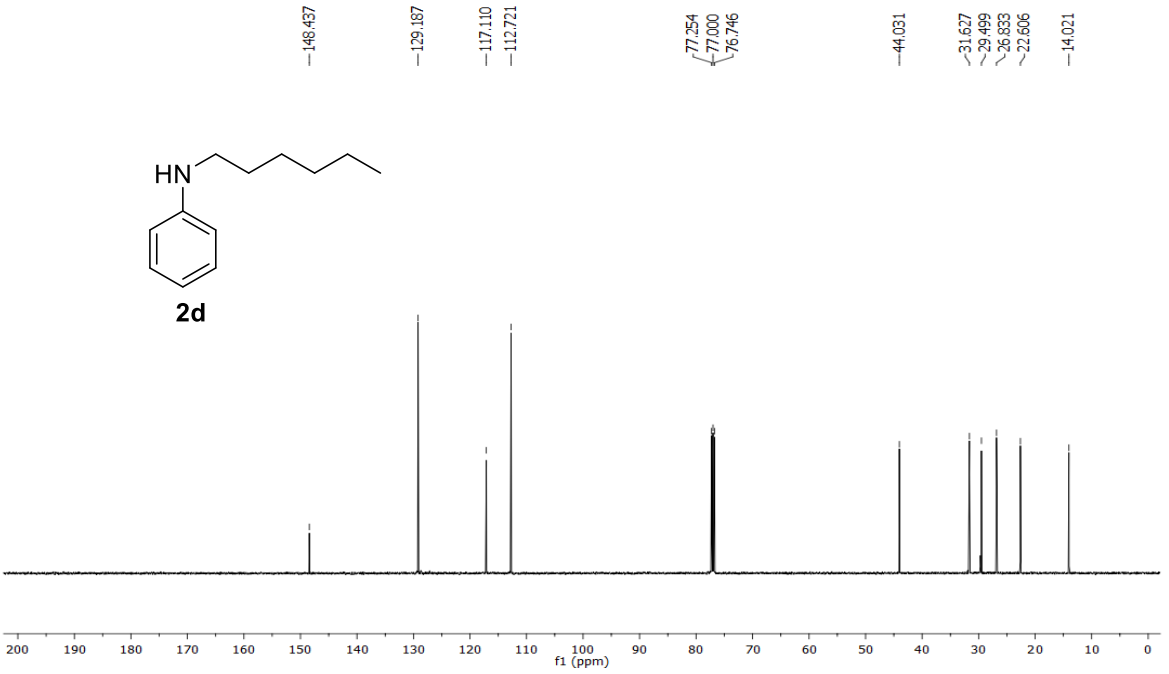


Figure 3.3. ^{13}C NMR Spectra of product 2d in $CDCl_3$

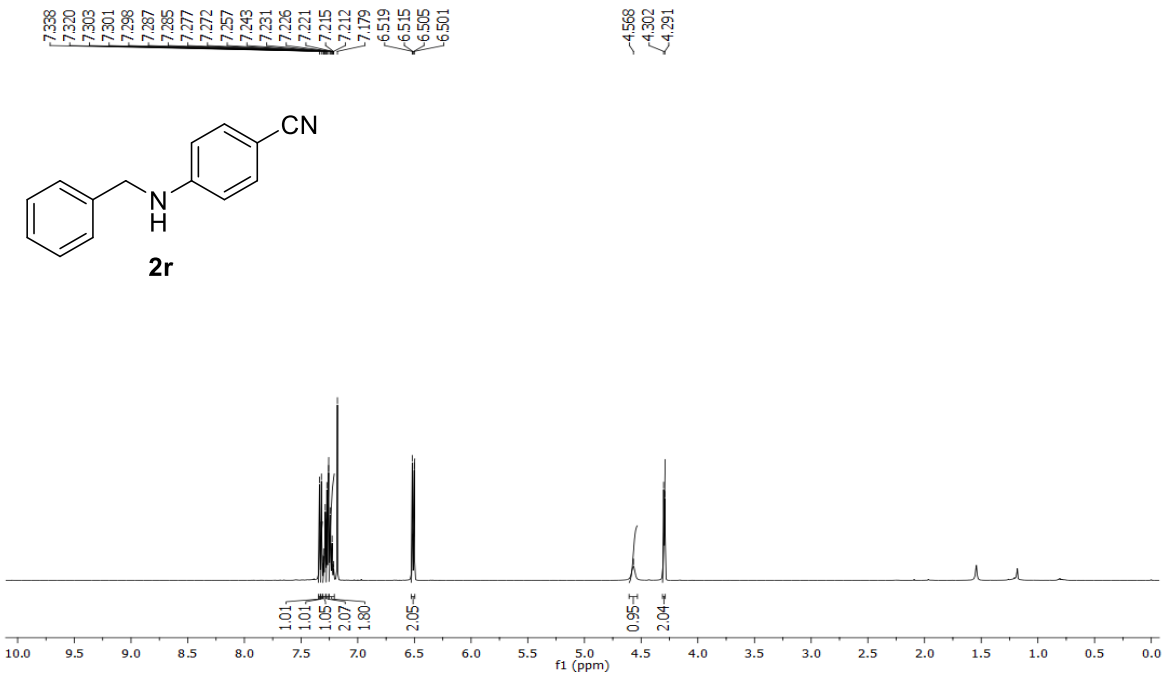


Figure 3.4. ^{1}H NMR Spectra of product 2r in $CDCl_3$

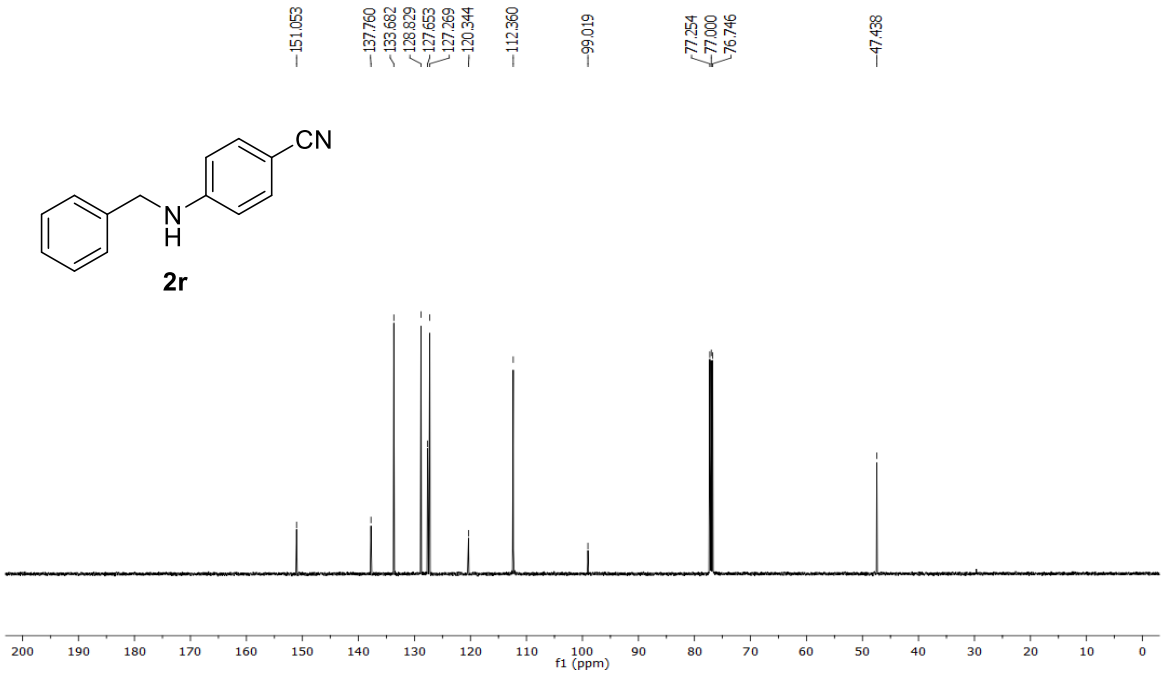


Figure 3.5. ^{13}C NMR Spectra of product 2r in $CDCl_3$

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