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Alternative method for the reduction of aromatic nitro to amine using TMDS-iron catalyst system

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ABSTRACT

The system 1,1,3,3-tetramethyldisiloxane (TMDS)/Fe(acac)$_3$ is reported here as a new method to obtain amines from aromatic nitro compounds. Amines are synthetized in a straightforward step and are isolated as hydrochloride salts with good to excellent yields. This system has shown a good selectivity toward aryl-chloride, aryl-bromide, ester, carboxylic acid, and cyano groups.

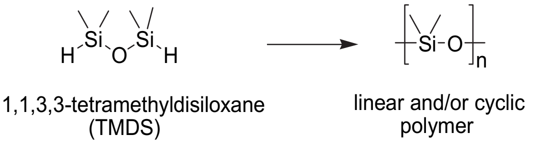
The reduction of alkylnitro compounds was unfortunately not possible using this method, only a mixture of mono and dialkylated amine was obtained.

1. Introduction

Amines are widely used in organic chemistry. They can be employed as a precursor and be transformed into several other groups (amides, imines, …). The development of new methods to access this function contained in a wide range of useful products is very important in organic chemistry.

Amines can be prepared by alkylation of ammoniac, reductive amination or by the reduction of amides, azides, nitriles or nitro functions. Conventional methods to reduce a nitro precursor use hydrogenation, electron-transfer, electrochemical, and hydride-transfer conditions.[1] In this field, Béchamp described in 1854 the first reduction of nitro functions to amines by iron.[2] Despite the efficiency of the method, the low cost and toxicity of iron, this technology presents a drawback: the use of a large excess of iron powder. Moreover the acidic medium of the reaction could not be compatible with many organic functions. In the same conditions, several other metals including cobalt,[3] zinc,[4] tin,[5] and molybdenum[6] have been used. The Béchamp process is still used in aniline plants however the major interest is the access to the colored iron oxide pigments obtained as co-product. Hydrogenation in the presence of homogenous or heterogeneous catalyst is the most common method used in industry for aromatic amines synthesis. Aniline is prepared efficiently both either the vapor or in the liquid phase in industrial processes. The metals employed in these reactions are palladium, nickel, rhodium, platinum, cobalt, and copper.[7] Depending on the support of the catalyst the chemoselectivity can be increased.[8]

Over the last decades, silanes have appeared to be new potential reducing agents when associated with metals. Thus they have been employed for the reduction of nitro functions using Re,[9] Pd,[10] Mo,[11] or Pt[12] catalysts with interesting results. Unfortunately, several silanes have been demonstrated harmful since they generate a dangerous, pyrophoric, and toxic SiH$_4$[13] gas. As a consequence, hydrosiloxanes having Si–O–Si bridge are considered as being a good alternative to silanes. Indeed, PMHS (polymethylhydrosiloxane),[14] a 40 units polymer, and TMDS (tetramethyldisiloxane) are safer since they are not known to release this dangerous gas. TMDS (Scheme 1) is a by-product of the silicon industry and the polymer by-product of the reaction can be recycled for the water-repellent treatment of materials. When associated with metals, such as Pd,[10] Pt,[15] Rh,[16] Re[9] or Ti,[17] PMHS, and TMDS can reduce carbonyl, amide, phosphine oxides, alkene, nitrile, sulfone functional groups.



Scheme 1. Structure of 1,1,3,3-tetramethyldisiloxane and its produced polymer by-product.

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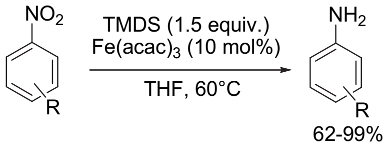
In the literature, only few articles relate the reduction of organic functionalities in the presence of environmentally begnin iron catalyst. Recently we have published the reduction of aromatic nitro compounds to the corresponding amines[18] using TMDS activated by a catalytic quantity of Fe(acac)$_3$ in THF at 60 °C (Scheme 2). During this work Nagashima[19] reported the reduction of amides to amines and he pointed out the high reactivity for the nitro group in the presence of an amide by the use of a catalytic system involving iron carbonyl and TMDS in toluene at 100 °C. The drawback of his methodology was the high temperature since the boiling point of TMDS is 71 °C. At the same time, Beller[20] also described the reduction of aromatic nitro compounds to amines with the Fe/PCy$_3$/PhSiH$_3$ system in the toluene at 110 °C. Herein we report a larger study for the reduction of the nitro function to amine with TMDS as reducing agent.



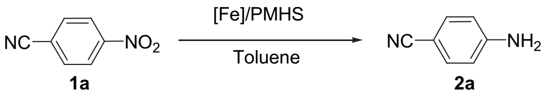
Scheme 2. Reduction of the nitro function to amine.

2. Results and discussion

2.1. Study of the experimental conditions

At the beginning of our investigation, different sources of iron were tested with PMHS as reducing agent using 4-nitrobenzonitrile **1a** as the model substrate. PMHS is easier to handle (high boiling point) and cheaper than TMDS. The reactions were realized in toluene at 90 °C (Table 1).

Table 1
Reduction of **1a** with different iron sources



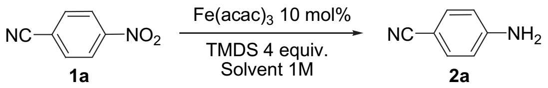
Entry	SiH	Si–H equiv	Catalyst	Mol % cat.	T °C	Conv.[a] (%)	Time h
1	PMHS	2	Fe(acac)$_3$	100	90	90	24
2		2	Fe(OAc)$_2$	100	90	44	24
3		4	FeCl$_3$	100	90	—	24
4		4	Fe(OAc)$_2$	10	90	—	24
5		4	Fe(acac)$_3$	10	90	55	24
6		4	Fe(acac)$_2$	10	90	51	15
7	TMDS	4	Fe(acac)$_3$	10	60	>98	48

[a] Determined by ^{1}H NMR.

The formation of the desired product were observed in the presence of PMHS with Fe(acac)$_3$ and Fe(OAc)$_2$ when stoichiometric quantities of iron were used (Table 1, entries 1 and 2). Nevertheless no conversion was observed with FeCl$_3$ (Table 1, entry 3). However when catalytic quantities of iron were used the reaction did not occur with Fe(OAc)$_2$ (Table 1, entry 4) and only Fe(acac)$_3$ and Fe (acac)$_2$ displayed interesting results (Table 1, entries 5 and 6). Although Fe(acac)$_2$ and Fe(acac)$_3$ have shown a similar reactivity, on an economical point of view we pursued the study with Fe(acac)$_3$. The partial conversions can be explained by the formation of an insoluble gel during the reaction that altered the reaction and made the isolation of the product difficult. This gel formation appeared to be the major drawback of PMHS.[21] Thus, a new source of hydrides, TMDS, was tested with Fe(acac)$_3$ in catalytic amount. The reaction occurred at 60 °C and a complete conversion was observed after 48 h (Table 1, entry 7). This interesting result led us to carry out our study with TMDS.

Different solvents were evaluated (Table 2). Because of the lower boiling point of TMDS (71 °C) compared to PMHS, tests were realized at lower temperature in order to avoid the use of sealed tubes. A test at room temperature has first been realized but after 36 h the conversion was less than 5%. Increasing the reaction temperature at 60 °C gave better results. The reaction was slower when performed in toluene (Table 2, entry 1), diethylcarbonate (Table 2, entry 4) or *t*-BuOH (Table 2, entry 5), whereas THF and MeTHF gave complete conversions after 24 h (Table 2, entries 2 and 3). MeTHF is more expensive than THF but is environmentally friendlier. Best conditions (Table 2, entry 2) have been selected.

Table 2
Evaluation of different solvents



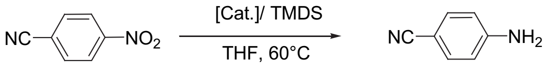
Entry	Solvent	T (°C)	Time h	Conv.[a] (%)
1	Toluene	60	48	>98
2	THF	60	24	>98
3	MeTHF	60	24	>98
4	DEC[b]	60	24	50
5	*t*-BuOH	60	4 days	>98

[a] Determined by ^{1}H NMR.
[b] Diethylcarbonate.

In order to improve the reaction time fluoride sources, such as CeF$_3$, TBAF, and KF have been tested to activate the siloxane[22] but no significant improvement was observed.

In order to verify if it was not an eventual presence of copper in the iron catalyst,[23] which catalyzed the reaction we tested the reduction with three copper catalysts (Table 3) in the THF at 60 °C. The low conversions with Cu(OAc)$_2$ (Table 3, entry 1), Cu(acac)$_2$ (Table 3, entry 2), and Cu(OMe)$_2$ (Table 3, entry 3) confirmed us that only the iron catalyzed the reduction of the nitro function. Based on Beller results concerning the effect of the ligand we added to copper acetate a ligand the triphenylphosphine. In this case, the triphenylphosphine have a positive effect on the reaction, probably the ligand stabilized the active species. These results led us to try the addition of PPh$_3$ with Fe(acac)$_3$. However no significant improvement was observed.

Table 3
Reduction of **1a** with copper salts



Entry	Catalyst	Mol % cat.	Ligand 30 mol %	Time h	Conv. (%)
1	Cu(OAc)$_2$	10	—	24	<10
2	Cu(acac)$_2$	10	—	24	<10
3	Cu(OMe)$_2$	10	—	24	<10
4	Cu(OAc)$_2$	10	PPh$_3$	24	85

Conversions were determined by TLC and ^{1}H NMR.

Hydrides stoichiometry. In our first investigation,[18] eight SiH/mol were added to the reaction mixture for the reduction of the nitro functionality to amine. In the theory only three hydrides are necessary to reduce the nitro, thus several experiments decreasing the quantity of TMDS have been realized (Table 4). It appeared that the

Table 4
Study of hydrides stoichiometry for the reduction of **1a**

Entry	TMDS (Si–H equiv)	Time h	Conv.[a] (%)
1	8	24	>98
2	6	24	>98
3	3	24	>98
4	2	24	60
5	1	40	30

Conditions: nitro compound **1a**, Fe(acac)$_3$ 10 mol %, TMDS, THF 1 M at 60 °C.
[a] Determined by ^{1}H NMR.

conversion was total with six SiH/mol of TMDS (Table 4, entry 2) and three SiH/mol (Table 4, entry 3), which are in agreement with the theory. Decreasing the amount of hydrides to 2 and then 1 (Table 4, entries 4 and 5), the conversions were not completed anymore. Moreover analysis confirms that the amine was formed and no intermediate, such as hydroxylamine was observed. These results could help for a study on a mechanism of the reaction.

2.2. Reduction of aromatic nitro

After these studies on the 4-nitrobenzonitrile **1a**, the best conditions (Table 2, entry 2) were applied on different nitroarenes (Table 5). All the reactions were carried out in nitrogen purged sealed tube or in a round bottom flask. Complete consumption of the starting material was followed by TLC or ^{1}H NMR. After complete conversion, reaction mixture was filtrated through a plug of Celite (top layer) and alumina (bottom layer) in a 1 cm diameter column by flushing with EtOAc. After concentration, the filtrate was diluted in a minimum of toluene and mixed with 1 M HCl. The aqueous layer was concentrated to afford the amine as the hydrochloride salt. This method of purification has been recently modified for a simplest one. Indeed after the dilution in a minimum of ether of the reaction mixture, 2 equiv of HCl in ether solution was added dropwise. After several minutes of stirring, a simple filtration was made to retrieve the precipitate washed several times with ether. The amine was isolated as the hydrochloride salt in high yields.

As depicted in Table 5, the reduction of aromatic nitro compounds was selective and efficient. When the nitroarene was substituted with a nitrile (Table 5, entry 1), only the nitro function was reduced to amine. For this substrate this method is selective in comparison with hydrogenation in the presence of supported platinium.[24] When nitroarenes were substituted with a bromine or a chlorine (Table 5, entries 3–6), no dehalogenated product was observed in comparison to hydrogenation in classical conditions with palladium on charcoal.[25] We, however, noticed a difference of reactivity between *meta*- and *ortho*-substituted nitroarene (Table 5, entries 3 and 4). The low reaction rate in the case of the *ortho*-bromonitrobenzene was probably due to a steric effect. In order to verify this hypothesis, the reduction was tested with the *para*-bromonitrobenzene since the electronic effects are similar for the *ortho* and the *para* positions. The product of reduction was obtained in 24 h and isolated with 80% yield. With other functionalities such as esters (Table 5, entry 7) or carboxylic acids (Table 5, entry 8) in the *para* position the reaction was selective and only the nitro group was reduced in amine. Surprisingly, when the nitroarene was substituted by an ester the reactivity was lower in comparison with the nitrile derivative. In order to obtain complete conversion, the reaction was performed in toluene at 90 °C (Table 5, entry 7). When the nitro compound was substituted in *para* by an aldehyde (Table 5, entry 9), we observed the reduction of the aldehyde. In this particular case, the aldehyde, substituted by a withdrawing group, was probably reduced first followed by the conversion of the nitro group to amine. The nitro group is important since Beller previously reported that Fe(acac)$_3$ was not a good catalyst for the reduction of benzaldehyde to alcohol.[26] Only 5% of alcohol was detected. For this compound Corma's conditions are more adapted.[8]

We were interested to test the reduction with an arene substituted by two nitro groups. In the case of the 1,4-dinitrobenzene (Table 5, entry 10), only one nitro was reduced to amine in 48 h. If the reaction was not stopped, in 72 h of reaction 30% of the diamine product were observed and no further conversion occurred. The same results were observed for the mono reduction of the 1,3-dinitrobenzene (Table 5, entry 11), however, the reduction of both nitro functions (Table 5, entry 12) was possible with a complete conversion in 24 h using 20 mol % of Fe(acac)$_3$ and 8 equiv of TMDS. The reduction with a methoxy group in the *para* position (Table 5, entry 13) occurred in 24 h and the desired product was isolated with 72% yield. When the arene was tri-substituted, conversion and yield were lower after 24 h of reaction. These results are probably due to the presence of a bromine (Table 5, entry 14) and a trifluoride group (Table 5, entry 15) in the *ortho* position. The reaction is easily implemented on a large scale since the reaction gave similar isolated yield when performed on 3 g (20.2 mmol). Analytical data of the prepared compound were compared to those of the literature.

Even when using a small amount of reagent the formation of intermediates was not observed. During the reaction the formation of the product and the starting material were observed. However in these conditions, when using phenylhydroxylamine as substrate we obtained aniline hydrochloride in 77% isolated yield in 24 h.

2.3. Preparation and reduction of aliphatic nitro

Some aliphatic nitro were prepared in order to study the scope and limitation of this reduction method. Nitro compounds can be prepared by the reaction between a bromide or iodide compounds and either sodium nitrite or silver nitrite in DMF. For an economic point of view we tested the preparation of aliphatic nitro using sodium nitrite.

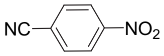
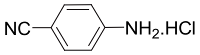
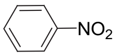
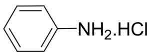
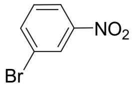
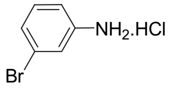
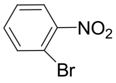
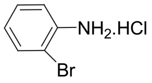
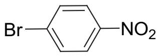
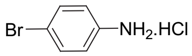
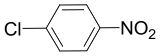
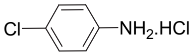
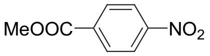
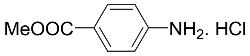
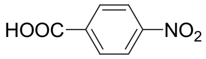
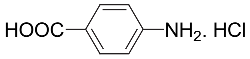
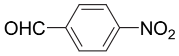
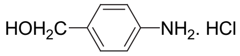
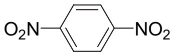
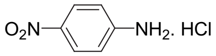
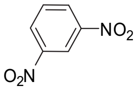
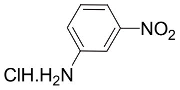
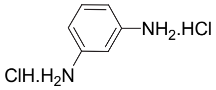
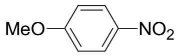
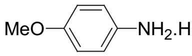
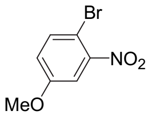
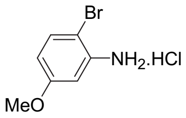
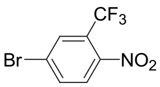
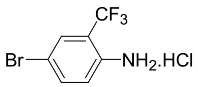
2.4. Method proposed by Kornblum[27]

Kornblum described the preparation of alkylnitro compounds by using 2 or 3 equiv of sodium nitrite with a halogenated compound. Although he obtained the desired product with moderate yields, he pointed out the formation of nitrite ester for the primary halides as major by-product. These conditions were tested on different primary alkylnitro but the isolated yields were not sufficient and the formation of the nitrite was fast. In order to optimize and to avoid the formation of a large quantity of the nitrite ester, the reaction was followed by GC every hour on 1-bromododecane at 0 °C. It appeared that after 7 h of reaction, 73% of the reagent was converted into a nitro compound and no nitrite ester was observed, whereas with the same conditions at room temperature Kornblum observed the formation of 29% of nitrite ester after 6 h.

The temperature of the reaction was maintained at 0 °C during the night and after an extraction, the crude product was obtained with 90% yield. A small quantity of nitrite ester, easily removed by flash chromatography, was observed.

The method for the reduction of the aromatic nitro compounds was then applied to the nitrododecane. Unfortunately, only a small quantity of the amine was detected by mass spectrometry and the major product was the didodecylamine. Although we dilute the reaction mixture and increase the amount of iron, we never obtained the isolated amine (Scheme 3). In order to verify if the low conversion was not due to the long chain, the reaction was tested on the nitroethane and the same results were obtained. The reduction was also tested on the *trans*-beta nitrostyrene, the desired product was not observed but the (2-nitroethyl)-benzene was

Table 5
Reduction of different nitro compounds to amines

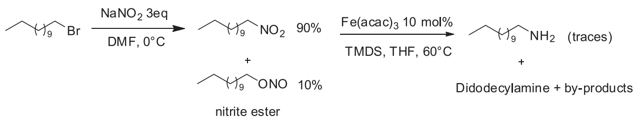
Entry	Substrates		Amines		Conversion (%)	Time (h)	Isolated yield (%)
1		**1a**		**2a**	100	24	92
2		**1b**		**2b**	100	24	>99
3		**1c**		**2c**	100	44	>99
4		**1d**		**2d**	44 85	24 48	n.d 66
5		**1e**		**2e**	100	24	80
6		**1f**		**2f**	100	48	>99
7		**1g**		**2g**	100	48	95[a]
8		**1h**		**2h**	87	24	62[b]
9		**1i**		**2i**	100	24	80[b]
10		**1j**		**2j**	100	48	95
11		**1k**		**2k**	100	48	98
12	**1k**			**2l**	100	24	>99[c]
13		**1m**		**2m**	100	24	72
14		**1n**		**2n**	30	24	25
15		**1o**		**2o**	46	24	20

Conditions: nitro compounds (2 mmol), Fe(acac)$_3$ (0.2 mmol), TMDS (1.5 equiv, 3 mmol), THF, 60 °C.
Conversions were determined with ^{1}H NMR. Isolated as hydrochlorides salts with >99% purity.

[a] Reaction was performed in toluene at 90 °C.

[b] Reaction was performed with 4 equiv of TMDS.

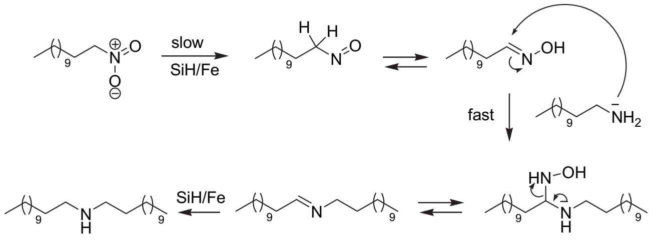
[c] Reaction performed with 20 mol % Fe(acac)$_3$ (0.4 mmol) and 8 equiv of TMDS (16 mmol).



Scheme 3. Preparation and reduction of aliphatic nitro compounds.

obtained. The double bond was reduced without any reduction of the nitro function.

The formation of the didodecylamine could be explained by the Nef type reaction[28] according to this proposition on the scheme below (Scheme 4):



Scheme 4. Formation of the didodecylamine.

The reaction was tested with an excess of TMDS in order to observe an eventual presence of aldehyde in the reaction mixture, which could react with the amine and form an oxime. Unfortunately the aldehyde was never observed.

3. Conclusion

We have developed a mild safe and efficient reduction procedure of the aromatic nitro function to amine. This method can constitute an alternative to the Béchamp procedure, which presented several drawbacks detailed above. The good selectivity and the easy reaction workup are an advantage since the method does not require purification by chromatography or distillation and the amine salts are pure (as judged by ^{1}H NMR and ^{13}C NMR).

4. Experimental section

4.1. General

All reagents were obtained commercially. Tetramethyldisiloxane, 97% (TMDS) was purchased from Acros, anhydrous THF from Aldrich, acetylacetonate iron (Fe(acac)$_3$), 99% from Strem Chemicals and the nitro compounds were supplied from Acros, Sigma—aldrich, and Alfa Aesar. All reagents and reactants were used without further purification. All reactions were performed under an inert atmosphere (argon) in a sealed tube except when the reaction was performed on 3 g. In this case the reaction was performed in a round bottom flask under inert atmosphere.

^{1}H NMR and ^{13}C NMR spectra were recorded on a BRUKER DRX 300 or BRUKER ALS 300 (except when mentioned) in MeOD and measurements are given in parts per million. Chemical shifts are given in ppm. General procedure for the reduction of nitro compounds.

In a solution of nitro compound (2 mmol) in 0.6 mL of THF were added Fe(acac)$_3$ (10 mmol %, 70 mg) and TMDS (1.5 equiv or three Si–H, 0.53 mL). After 24 h (unless otherwise indicated) under heating the reaction mixture was diluted in a minimum of Et$_2$O with a constant stirring. HCl (2 equiv) in Et$_2$O was then added dropwise. A precipitate appears; the mixture was stirred for 5 min and filtered. It was washed several times with Et$_2$O and dried to afford the desired product as a hydrochloride salt.

*4.1.1. Aniline hydrochloride (**2a**) [142–04–1].* ^{1}H NMR: 7.55 (m, 3H), 7.41 (d, 2H, J=6.8 Hz). ^{13}C NMR (75 MHz, MeOD, δ ppm): 132.3, 132.0, 130.9, 124.8. EIMS m/z (% relative abundance): 93 $[M]^{+\bullet}$. IR ν_{max}: 2814, 2569, 1489, 740, 685. Brown solid, 258 mg, >99%. Mp: 189 °C.

*4.1.2. 3-Bromoaniline hydrochloride (**2b**) [56,967–17–0].* ^{1}H NMR: 7.64 (d, 1H, J=8.3 Hz), 7.56 (s, 1H), 7.45 (t, 1H, J=8.0 Hz), 7.35 (d, 1H=8.0 Hz). ^{13}C NMR: δ=134.0, 133.9, 133.7, 128.0, 124.6, 124.0. EIMS m/z (% relative abundance): 171 $[M]^{+\bullet}$, 173 $[M]^{+\bullet}$. IR ν_{max}: 2869, 2563, 1553, 1472, 1071, 783, 672. Brown solid, 380 mg, >99%. Mp: 177 °C.

*4.1.3. 2-Bromoaniline hydrochloride (**2c**) [94,718–79–3].* ^{1}H NMR: 7.79 (d, 1H, J=7.8 Hz), 7.47 (m, 2H,), 7.37 (d, 1H, J=8.0 Hz). ^{13}C NMR (100 MHz, MeOD, δ ppm): 136.0, 132.8, 131.7, 131.5, 126.8, 118.4. EIMS m/z (% relative abundance): 171 $[M]^{+\bullet}$, 173 $[M]^{+\bullet}$. IR ν_{max}: 2797, 2575, 1471, 751. Brown solid, 276 mg, 66%. Mp: 163 °C.

*4.1.4. 4-Bromoaniline hydrochloride (**2d**) [624–19–1].* ^{1}H NMR: 7.74 (d, 2H, J=8.8 Hz), 7.35 (2, 2H, J=8.8 Hz). ^{13}C NMR: 134.9, 131.6, 127.0, 124.2. EIMS m/z (% relative abundance): 171.9 $[M+H]^{+}$, 173.9 $[M+H]^{+}$. IR ν_{max}: 2845, 2566, 1564, 1484, 1116, 1070, 1016, 815. Beige solid, 335 mg, 80%. Mp: 190 °C.

*4.1.5. 4-Chloroaniline hydrochloride (**2e**) [20,265–96–7].* ^{1}H NMR: δ=7.57 (d, 2H, J=8.5 Hz), 7.39 (d, 2H, J=8.7 Hz). ^{13}C NMR: 136.2, 132.2, 130.9, 127.0. EIMS m/z (% relative abundance): 127 $[M]^{+\bullet}$, 129 $[M]^{+\bullet}$ (33%). IR ν_{max}: 2808, 2602, 2571, 1488, 1092, 1010, 818. Brown solid, 326 mg, >99%. Mp: 194 °C.

*4.1.6. 4-Cyanoaniline hydrochloride (**2f**) [2570–98–1].* ^{1}H NMR: (300 MHz, MeOD, δ ppm): 7.63 (d, 2H, J=8.5 Hz), 7.10 (d, 2H, J=8.3 Hz). ^{13}C NMR (100 MHz, MeOD, δ ppm): 137.8, 135.2, 124.3, 111.6. EIMS m/z (% relative abundance): 118 $[M]^{+\bullet}$. IR ν_{max} (cm^{-1}): 2800, 2544, 2235, 1606, 1501, 833. Light brown solid, 285 mg, 92%. Mp: 168 °C.

*4.1.7. Methyl-4-aminobenzoate hydrochloride (**2g**) [63,450–84–0].* ^{1}H NMR: 7.85 (d, 2H, J=8.7 Hz), 6.64 (d, 2H, J=8.8 Hz). ^{13}C NMR: 170.2, 155.6, 133.3, 119.4, 115.2, 52.8. EIMS m/z (% relative abundance): 151 $[M]^{+\bullet}$ 120 $[M]^{+\bullet}$–OMe. IR ν_{max}: 2860, 1720, 1703, 1316, 1109, 755. White solid, 360 mg, 95%. Mp: 121 °C.

*4.1.8. 4-Aminobenzoic acid hydrochloride (**2h**) [22,669–27–8].* ^{1}H NMR: 8.10 (d, 2H, J=8.3 Hz), 7.36 (d, 2H, J=8.0 Hz). ^{13}C NMR: 168.4, 137.1, 133.0, 132.2, 124.6. EIMS m/z (% relative abundance): 137 $[M]^{+\bullet}$, 120 $[M]^{+\bullet}$–OH. IR ν_{max}: 2892, 1576, 1521, 1507, 1245, 1110, 755, 741. White solid, 253 mg, 73%. Mp: 227 °C.

*4.1.9. (4-Aminophenyl)-methanol hydrochloride (**2i**) [170,926–25–7].* ^{1}H NMR: 7.56 (d, 2H, J=8.5 Hz), 7.40 (d, 2H, J=8.7 Hz), 4.69 (1, 2H). ^{13}C NMR: 141.6, 131.2, 130.5, 124.9, 75.4. EIMS m/z (% relative abundance): 123 $[M]^{+\bullet}$, 122 $[M^{+\bullet}–H^{\bullet}]^{+}$, 106 $[M^{+\bullet}–OH^{\bullet}]^{+}$. IR ν_{max}: 1587, 1563, 1538, 1330, 1168, 1015, 798. Black solid, 250 mg, 80%. Mp: >250 °C.

*4.1.10. 4-Nitroaniline hydrochloride (**2j**) [15,873–51–5].* ^{1}H NMR: 8.21 (d, 2H, J=8.7 Hz), 7.17 (d, 2H, J=8.8 Hz). ^{13}C NMR: 142.8, 141.6, 127.1, 123.6. EIMS m/z (% relative abundance): 139 $[M+H]^{+}$. IR ν_{max}: 2808, 2558, 1595, 1520, 1347, 1323, 1133, 1110, 860, 741. Brown solid, 331 mg, 95%. Mp: 156 °C.

*4.1.11. 3-Nitroaniline hydrochloride (**2k**) [33,240–96–9].* ^{1}H NMR: 8.19 (d, 1H, J=8.3 Hz), 8.12 (s, 1H), 7.71 (t, 1H, J=8.2 Hz), 7.64 (d, 1H, =9.0 Hz). ^{13}C NMR: 149.4, 134.2, 132.9, 131.5, 125.3, 119.5. EIMS m/z (% relative abundance): 139 $[M+H]^{+}$. IR ν_{max}: 2819, 2572, 1541, 1530, 1488, 1350, 1093, 732. Brown solid, 341 mg, 98%. Mp: 166 °C.

*4.1.12. 1,3-Diaminobenzene hydrochloride (**2l**) [541–69–5].* ^{1}H NMR: 7.54 (t, 1H, J=8.2 Hz), 7.23 (d, 2H, J=8.2 Hz), 7.21 (s, 1H). ^{13}C NMR: (75 MHz, D$_2$O) 132.8, 132.2, 124.9, 119.2. EIMS m/z (% relative abundance): 109 $[M+H]^{+}$. IR ν_{max}: 2806, 2584, 1528, 1487, 1100, 671. Brown solid, 287 mg, >99%. Mp: >250 °C.

*4.1.13. 4-Methoxyaniline hydrochloride (**2m**) [20,265–97–8].* ^{1}H NMR: 7.34 (d, 2H, J=9.0 Hz), 7.10 (d, 2H, J=9.1 Hz), 3.86 (s, 3H). ^{13}C NMR: 126.1, 117.2, 57.0. EIMS m/z (% relative abundance): 124 $[M+H]^{+}$. IR ν_{max}: 2837, 2590, 1510, 1267, 1172, 1023, 835. Blue solid, 230 mg, 72%. Mp: 182 °C.

*4.1.14. 2-Bromo-5-methoxyaniline hydrochloride (**2n**) [129,968–11–2].* ^{1}H NMR: 7.64 (d, 2H, J=8.9 Hz), 7.00 (s, 1H), 6.94 (d, 2H,

J=8.9 Hz), 3.86 (s, 3H). ^{13}C NMR: 162.1, 136.3, 132.7, 118.2, 112.9, 108.7, 57.6. EIMS m/z (% relative abundance): 202 [M+H]$^+$, 204 [M+H]$^+$. IR ν_{max}: 2736, 2525, 1544, 1478, 1325, 1248, 1169, 1013, 846, 823. Beige solid, 125 mg, 27%. Mp: 162 °C.

*4.1.15. 4-Bromo-2-trifluoromethylaniline hydrochloride (**2o**) [1,214,372–39–0].* ^{1}H NMR: 7.58 (s, 1H), 7.50 (d, 2H, J=8.9 Hz), 6.92 (d, 2H, J=8.6 Hz). ^{13}C NMR: 138.9, 134.0, 132.1, 127.5, 126.1, 124.4 (q, 1C, J_{C-F3}=34.5 Hz), 123.3, 120.7. EIMS m/z (% relative abundance): 240 [M+H]$^+$, 242 [M+H]$^+$. IR ν_{max}: 2768, 2488, 1487, 1300, 1122, 839. Orange solid, 110 mg, 20%. Mp: 114 °C.

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