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$Pd(OAc)_2$-catalyzed dinitration reaction of aromatic amines

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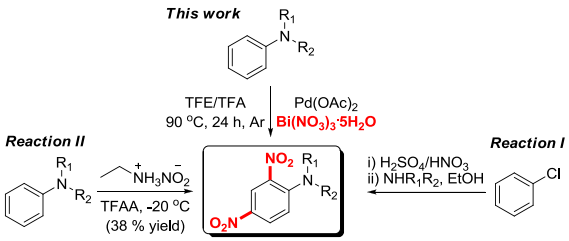
ABSTRACT

Taking advantage of $Pd(OAc)_2$-catalyzed dinitration reactions with $Bi(NO_3)_3\cdot 5H_2O$ in trifluoroethanol (TFE) and trifluoroacetic acid (TFA), we have developed an efficient and practical method for the synthesis of secondary dinitro-aromatic amines. The products could be applied to the preparation of 5-amine-*N*-methyl-benzimidazolone, the azo-dyes, economic advantages. The method has also been expanded to the dinitration reaction of some tertiary aromatic amines.

1. Introduction

Dinitro-aromatic compounds are crucial intermediates for the production of industrially chemicals,[1] such as dyes, pharmaceuticals and fragrances.[2,3] Among them, dinitro-aromatic amines were also applied as the energetic materials in the civilian field. However, traditional methods for the dinitration, the use of mixed acid (HNO_3/H_2SO_4), could not be applied for the preparation of dinitro-aromatic amines, because conventional mixed acid has oxidizing activity and destroys the substrates.[4] To obtain dinitro-aromatic amines compounds, a common and indirect technology had been applied: i) the synthesis of 2,4-dinitrochlorobenzene that using mixed acid as nitration reagent; ii) the substitution reaction of 2,4-dinitrochlorobenzene, such as Piersanti et al.[5] reported, with secondary amines (Scheme 1, reaction I). Moreover, Laali et al. reported the dinitration of aniline using ethylammonium nitrate (EAN) as the nitration reagent (Scheme 1, reaction II).[6] However, this method suffers from some limitations such as low yield as well as harsh reaction conditions. Thus the development of efficient and straightforward protocols for dinitration of aromatic amines is still a distinct challenge. Herein, we report a $Pd(OAc)_2$-catalyzed[7] dinitration of aromatic amines with $Bi(NO_3)_3\cdot 5H_2O$[8,9] as dinitration reagent in the mixture of TFE/TFA[10] to give dinitro-aromatic amines (Scheme 1). We provided higher yields and more economical method in this work, and the products could be applied in the synthesis of the intermediates of azo-dyes.



Scheme 1. 2,4-Dinitration of aromatic amines.

2. Results and discussion

In the initial experimental protocol, we selected *N*-ethylaniline as the substrate to optimize the reaction conditions and tested different solvents (2 mL) under Ar at 70 °C (Table 1, entries 1–5). A promising result showed that TFA as one of the solvents played an important role, and the desired product was obtained in better yield (Table 1, entry 5). Encouraged by this favorable result, we carried out some further investigation of the reaction medium, and a mixed solvent of TFE and TFA with a volume ratio of 3/1 (TFE/TFA=3/1) obtained a better result in terms of yield at 90 °C for 24 h (Table 1, entries 6–12). However, the result showed that the yield would decrease with the increase of reaction temperature (Table 1,

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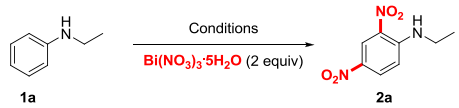
Table 1
Screening of the reaction conditions[a]



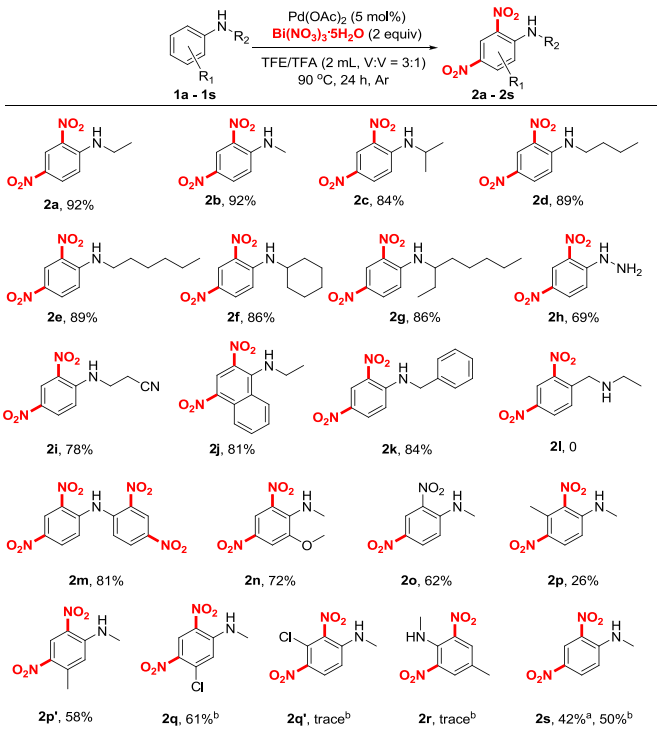
Entry	Catalyst (mol %)	T/°C	t/h	Solvent	Yields (%)[b]
1	—	70	24	dioxane	0
2	—	70	24	TFE	0
3	—	70	24	dioxane/HOAc	11
4	—	70	24	TFE/HOAc	25
5	—	70	24	TFE/TFA	48
6	—	70	16	TFE/TFA	30
7	—	70	32	TFE/TFA	45
8[c]	—	70	24	TFE/TFA	35
9[d]	—	70	24	TFE/TFA	44
10[e]	—	70	24	TFE/TFA	28
11	—	70	24	TFA	trace
12	—	90	24	TFE/TFA	56
13	—	100	24	TFE/TFA	47
14	CuI (10)	90	24	TFE/TFA	68
15	CuBr (10)	90	24	TFE/TFA	61
16	CuCl (10)	90	24	TFE/TFA	58
17	$PdCl_2$ (10)	90	24	TFE/TFA	77
18	$Pd(acac)_2$ (10)	90	24	TFE/TFA	74
19	$Pd(OAc)_2$ (10)	90	24	TFE/TFA	93
20[f]	$Pd(OAc)_2$ (5)	90	24	TFE/TFA	92
21[g]	$Pd(OAc)_2$ (3)	90	24	TFE/TFA	76
22[h]	$Pd(OAc)_2$ (5)	90	24	TFE/TFA	27
23[i]	$Pd(OAc)_2$ (5)	90	24	TFE/TFA	90
24	$Ce(OAc)_3$ (10)	90	24	TFE/TFA	71
25	$FeCl_3$ (10)	90	24	TFE/TFA	67
26	$Co(OAc)_2$ (10)	90	24	TFE/TFA	75
27	$Co(acac)_2$ (10)	90	24	TFE/TFA	60
28	$Ni(NO_3)_3$ (10)	90	24	TFE/TFA	57

[a] Reaction conditions: **1a** (0.3 mmol), $Bi(NO_3)_3 \cdot 5H2O$ (2 equiv, 0.6 mmol), solvent (2 mL), stirring 15 min at room temperature (rt) firstly, heated with stirring under Ar finally.
[b] Isolated yields based on silica gel column chromatography separation. The ratio of the mixed solvents was volume of 3: 1 (entries 3–7, entries 12–23).
[c] TFE:TFA (1:1, 2 mL).
[d] TFE: TFA (4:1, 2 mL).
[e] TFE: TFA (7:1, 2 mL). Entries 14–16 were Cu-catalysts (0.03 mmol, 10 mol %). Entries 17–19 were Pd-catalysts (0.03 mmol, 10 mol %).
[f] $Pd(OAc)_2$ (0.015 mmol, 5 mol %).
[g] $Pd(OAc)_2$ (0.009 mmol, 3 mol %).
[h] $Bi(NO_3)_3 \cdot 5H_2O$ (1 equiv, 0.3 mmol).
[i] $Bi(NO_3)_3 \cdot 5H_2O$ (3 equiv, 0.9 mmol).

entries 12–13), presumably these were caused by the temperature is above the boiling point of solvent excessively.

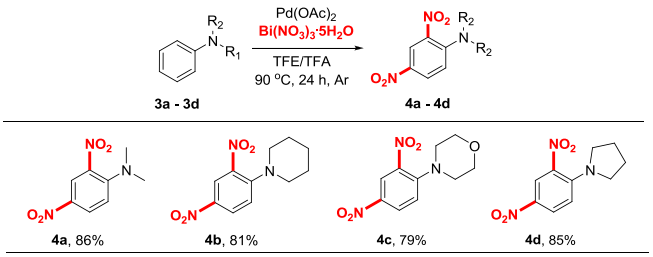
In comparison with the Cu-catalysts, experimental results showed that Pd-catalysts exhibited better activity (Table 1, entries 14–17). Some other Pd-catalysts were then examined under the reaction conditions. For example, $PdCl_2$ and $Pd(acac)_2$ afforded moderate yields of the desired product, $Pd(OAc)_2$ afforded best yields with the catalytic amount of 10 mol % (entries 17–19). Therefore it would be concluded that $Pd(OAc)_2$ was the most appropriate catalyst for this reaction. Taking into almost the same yields with 10 mol % and 5 mol % $Pd(OAc)_2$, we would select 5 mol % $Pd(OAc)_2$ in next expansion reactions, which was in accordance with environmental and economic guidelines (entries 19–20). We tried two control experiments to verify whether the dosage of $Bi(NO_3)_3 \cdot 5H_2O$ would impact on the yields of the reaction (Table 1, entries 22–23). The results manifested that 0.5 equiv of $Bi(NO_3)_3 \cdot 5H_2O$ would drop the yield of **2a** significantly to 27% (Table 1, entry 22) and the use of 3.0 equiv $Bi(NO_3)_3 \cdot 5H_2O$ did not improve the yield of **2a** efficiently (Table 1, entry 23). Finally, we tested some other metal catalyst, but the product yield was unfavorable (Table 1, entries 24–28).

With the optimal reaction conditions in hand, different kinds of secondary aromatic amines were set out to explore the reaction scope (Scheme 2). *N*-alkylanilines reacted with $Bi(NO_3)_3 \cdot 5H_2O$ to obtain the corresponding 2,4-dinitro-secondary aromatic amines in high yields (**2a**–**2g**). Not only *N*-alkylanilines, but also **1h** and **1i** could participate in this reaction condition to obtain the expected products in moderate to good yields (**2h**–**2i**). Besides, with **1j** as a substrate, the corresponding product (**2j**) was obtained in 81% yield. As shown in Scheme 2, the yield of 2,4-dinitro-*N*-benzylaniline was good (**2k**, 84%). By contrast, **1l** was examined, the result demonstrated that dinitration reaction would not happen (**2l**). Furthermore, **1m** was tested with the use of 4 equiv $Bi(NO_3)_3 \cdot 5H_2O$, and the final product was 2,4-dinitration on both rings dramatically (**2m,** 81%). In the next work, the introduction of electron-donating and electron-withdrawing groups on aniline core provided for different results significantly. In simple terms, the dinitro-aromatic amines bearing electron-withdrawing groups were found to be lower yields than the ones bearing electron-donating groups (**2n**–**2s**). The dinitration of **1n** afforded **2n** in high yield relatively (72%), but nitro group (**1o**) decreased the yield to 62% (**2o**), most likely due to the passivation effect of the electron-withdrawing group. The results of *meta*-substituted aromatic amines were very interesting, two diffident *ortho*-positions on aniline core would be substituted in this reaction, and the dinitro-aromatic amines bearing electron-donating groups were showed to be higher yields (**2p**–**2p′**, **2q**–**2q′**). With the use of 4-methyl-*N*-methylaniline (**1r**), whose para position is occupied, we only separated 4-methyl-2, 5-dinitro-*N*-methylaniline as the product in trace (**2r**). When 4-Br-*N*-methylaniline (**1s**) was tested, 2,4-dinitro-*N*-methylaniline was obtained, whose *para*-bromo was substituted by nitro group, with yield of 50% (**2s**), probably due to the passivation effect of nitro group.



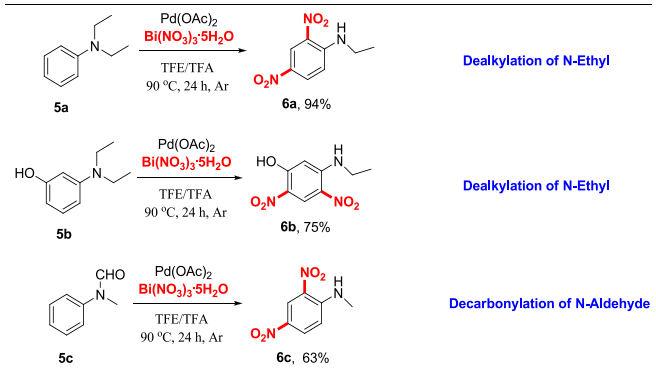
Scheme 2. Dinitration reactions of secondary aromatic Amines. Reactions were carried out using 1 equiv imino-anilines (0.3 mmol), 2 equiv $Bi(NO_3)_3 \cdot 5H_2O$ (0.6 mmol), 5 mol % $Pd(OAc)_2$, TFE/TFA (2 mL, V:V=3:1) as solvent, heated at 90 °C for 24 h under Ar. $Pd(OAc)_2$ (0.03 mmol, 10 mol %).

To test the anilines generality and limitations of this reaction, some tertiary aromatic amines were investigated. Compared to secondary amines, 2,4-dinitration of tertiary amines was difficult. Here only four substrates to give the corresponding products, but good yields (79–86%) were obtained in this dinitration reaction (Scheme 3, **4a**–**4d**).



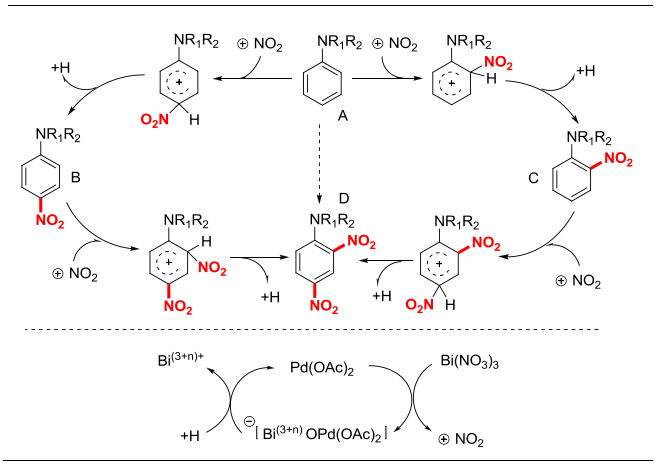
Scheme 3. Expanding 2,4-dinitration reactions of tertiary aromatic amines. Reactions were carried out using 1 equiv nitrilo-anilines (0.3 mmol), 2 equiv $Bi(NO_3)_3{\cdot}5H_2O$ (0.6 mmol), 5 mol % $Pd(OAc)_2$, TFE/TFA (2 mL, V:V=3:1) as solvent, heated at 90 °C for 24 h under Ar.

As to some tertiary amines, we had obtained unanticipated results. For instance, the reaction of **5a** afforded 2,4-dinitro-*N*-ethylaniline in yield of 94% (**6a**), due to the corresponding product was removed one of the *N*,*N*-diethyl groups. At the same time two other tertiary amines had also been dealkylated (**6b**) and decarbonylated products (**6c**). In order to make a further investigation, we changed 1,4-dioxane/TFA (3/1, 2 mL) instead and also obtained dealkylated products in a lower yield. According to Teuten explained, it was oxidation and hydrolysis process. Tertiary amine nitrogen cation intermediate was formed after conversion, and α-carbon of *N*-alkyl deprotonated to obtain the corresponding carbon radical, then carbon radical was oxidized to generate an iminium ion, which was hydrolyzed in the media to obtain secondary amine finally. Moreover, this conversion preferred to select deethylation rather than methyl in a relatively acid system.[11] This interpretation was consistent with our experimental results indeed and explained why *N*,*N*-dimethylaniline is vague and confusing (Scheme 2, **4a**). Scheme 4.



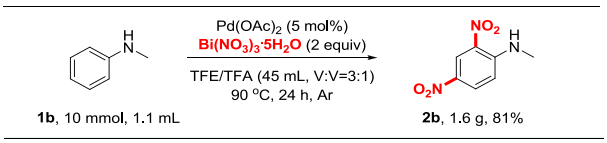
Scheme 4. N-dealkylation of 2,4-dinitration reactions. Reactions were carried out using nitrilo-anilines 1 equiv (0.3 mmol), $Bi(NO_3)_3{\cdot}5H_2O$ 2 equiv (0.6 mmol), $Pd(OAc)_2$ 5 mol %, TFE/TFA (2 mL, V:V=3:1) as solvent was heated at 90 °C for 24 h under Ar.

As illustrated in Scheme 5 , we propose the dinitration mechanism about Lewis acid catalyzed electrophilic aromatic substitution. Owing to the orientation effect of amine group, aromatic amines will be converted to the intermediates of *o*-nitration and *p*-nitration firstly, and then we expect that the intermediates are substituted by a second nitryl to obtain the dinitration products rapidly. In order to verify the possibility of the mechanism, *N*-methylaniline (**1b**) as substrate was heated at 90 °C for 1 h under Ar, we have successfully isolated the *N*-methyl-2-nitroaniline and *N*-methyl-4-nitroaniline, and simultaneously obtain the dinitro product. Therefore, the validation experiments suggest the pathway in Scheme 5 is reasonable.



Scheme 5. Proposed mechanism for dinitration of aromatic amines.

To further probe the application to Pd-catalyzed dinitration in preparative organic synthesis, a gram-scale reaction was carried out. As depicted in Scheme 6, *N*-methylaniline (**1b**) was amplified to 10 mmol, 1.6 g **2b** (81% yield) was successfully obtained.



Scheme 6. Gram-scale Synthesis of *N*-methyl-2,4-dinitroaniline. Reactions were carried out using **1b** 1 equiv (10 mmol), $Bi(NO_3)_3{\cdot}5H_2O$ 2 equiv (20 mmol), $Pd(OAc)_2$ 5 mol %, TFE/TFA (45 mL, V:V=3:1) as solvent was heated at 90 °C for 24 h under Ar.

3. Conclusion

In summary, we have established an efficient and direct method for the preparation of dinitro-compounds from aromatic amines with high yields, without the protection of amine groups. Our protocol is broad in dinitration of aromatic amine compounds, both secondary and tertiary compounds can be used.

4. Experimental section

4.1. General procedures for dinitration of aromatic amines

$Bi(NO_3)_3{\cdot}5H_2O$ (2 equiv, 0.6 mmol), $Pd(OAc)_2$ (0.015 mmol, 5 mol %) were added into a 25 mL oven-dried Schlenk tube, the tube was evacuated and backfilled with Ar (repeated three times in 30 min). Under a counter flow of Ar, *N*-substituted aniline (1 equiv, 0.3 mmol) was added by syringe firstly, 1.5 mL TFE and 0.5 mL TFA were then added by disposable medical syringes. The flask was sealed and the mixture was stirred firstly at room temperature for 15 min, then allowed to stir in a preheated oil bath at 90 °C for 24 h. The mixture was cooled to room temperature when the reaction was completed. Next, the solution was diluted by 10 mL ethyl acetate and filtered the insoluble matters, washed the organic phases by 5% $NaHCO_3$ solution after the extraction, and extracted the aqueous phases by ethyl acetate (3×15 mL) to collect organic phases. All the organic solutions were washed by brine, dried 30 min with anhydrous $MgSO_4$, filtered and concentrated under

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reduced pressure. The crude products were purified by chromatography on silica gel, eluting with ethyl acetate/petroleum ether (5/1-2/1).

4.1.1. 2,4-Dinitro-N-ethylphenylamine ***(2a)***.[12] Following general procedure, yellow solid (92%, 58.3 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.13 (d, J=2.2 Hz, 1H), 8.50 (s, 1H), 8.27 (dd, J=9.5, 2.5 Hz, 1H), 6.91 (d, J=9.5 Hz, 1H), 3.47 (dt, J=14.4, 7.2 Hz, 2H), 1.43 (t, J=7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.20, 135.81, 130.30, 126.30, 124.28, 113.84, 38.32, 14.04. Mp 111–112 °C (lit.[12] 112–114 °C).

4.1.2. N-Methyl-2,4-dinitroaniline ***(2b)***.[13,17] Following general procedure, brown-red solid (92%, 54.4 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (d, J=2.5 Hz, 1H), 8.57 (s, 1H), 8.30 (dd, J=9.5, 2.3 Hz, 1H), 6.92 (d, J=9.5 Hz, 1H), 3.15 (d, J=5.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.11, 136.10, 130.41, 124.23, 113.51, 30.24. Mp 172–174 °C (lit.[21a] 171 °C).

4.1.3. N-Isopropyl-2,4-dinitroaniline ***(2c)***.[12] Following general procedure, yellow solid (84%, 56.8 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.13 (d, J=2.6 Hz, 1H), 8.50 (s, 1H), 8.25 (dd, J=9.6, 2.6 Hz, 1H), 6.92 (d, J=9.6 Hz, 1H), 3.93 (dq, J=13.1, 6.5 Hz, 1H), 1.39 (d, J=6.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.47, 135.56, 130.25, 130.02, 124.54, 114.09, 44.96, 30.94, 22.39. Mp 93–95 °C (lit.[21b] 94 °C).

4.1.4. N-Butyl-2,4-dinitroaniline ***(2d)***.[14] Following general procedure, yellow solid (89%, 63.9 mg)[1]; H NMR (600 MHz, $CDCl_3$) δ 9.14 (d, J=2.6 Hz, 1H), 8.55 (s, 1H), 8.26 (dd, J=9.5, 2.6 Hz, 1H), 6.92 (d, J=9.5 Hz, 1H), 3.41 (td, J=7.1, 5.3 Hz, 2H), 1.76 (dt, J=12.9, 7.4 Hz, 2H), 1.50 (dq, J=14.8, 7.4 Hz, 2H), 1.00 (t, J=7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.36, 135.84, 130.28, 124.32, 113.87, 43.29, 30.66, 20.10, 13.64. Mp 88–90 °C (lit.[21c] 89–90 °C).

4.1.5. N-Hexyl-2,4-dinitroaniline ***(2e)***. Following general procedure, yellow solid (89%, 71.4 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.08 (d, J=2.6 Hz, 1H), 8.54 (s, 1H), 8.23 (dd, J=9.3, 2.4 Hz, 1H), 6.91 (d, J=9.5 Hz, 1H), 3.40 (td, J=7.2, 5.4 Hz, 2H), 1.76 (dt, J=15.0, 7.4 Hz, 2H), 1.49–1.41 (m, 2H), 1.38–1.27 (m, 4H), 0.89 (t, J=7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.33, 135.74, 130.21, 124.22, 113.89, 43.56, 31.26, 28.57, 26.51, 22.41, 13.88. HRMS calcd for $C_{12}H_{17}N_3O_4$ (M+): 267.1219; found: 267.1222. Mp 51–53 °C (lit.[21d] 52 °C).

4.1.6. N-Cyclohexyl-2,4-dinitroaniline ***(2f)***.[12] Following general procedure, yellow solid (86%, 68.4 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (d, J=2.4 Hz, 1H), 8.60 (s, 1H), 8.23 (dd, J=9.5, 2.6 Hz, 1H), 6.92 (d, J=9.6 Hz, 1H), 3.59 (s, 1H), 2.11–2.03 (m, 2H), 1.83 (t, J=6.6 Hz, 2H), 1.61 (d, J=66.5 Hz, 2H), 1.45 (t, J=9.8 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.45, 135.59, 130.17, 124.64, 114.16, 51.86, 32.39, 31.90, 29.67, 25.26, 24.32. Mp 153–155 °C (lit.[12] 155 °C).

4.1.7. N-(1-Ethylhexyl)-2,4-dinitroaniline ***(2g)***. Following general procedure, brown-red liquid (86%, 76.2 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.10 (dd, J=4.1, 2.6 Hz, 1H), 8.62 (s, 1H), 8.24 (d, J=9.4 Hz, 1H), 6.92 (d, J=9.6 Hz, 1H), 3.31 (t, J=5.7 Hz, 2H), 1.74–1.70 (m, 1H), 1.47 (dd, J=13.6, 7.0 Hz, 2H), 1.44–1.37 (m, 2H), 1.34–1.29 (m, 4H), 0.94 (t, J=7.4 Hz, 3H), 0.89 (dd, J=6.9, 5.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.55, 135.72, 130.26, 124.27, 113.88, 46.55, 38.70, 31.09, 28.74, 24.42, 22.84, 13.92, 10.81. HRMS calcd for $C_{14}H_{21}N_3O_4$ (M+): 295.1532; found: 295.1536.

4.1.8. 2,4-Dinitrophenylhydrazine ***(2h)***.[15] Following general procedure, brown-red solid (69%, 41.0 mg); ^{1}H NMR (600 MHz, DMSO) δ 9.95 (s, 1H), 8.74 (d, J=2.7 Hz, 1H), 8.18 (ddd, J=9.7, 2.7, 0.7 Hz, 1H), 7.62 (d, J=9.7 Hz, 1H), 4.99 (s, 2H). ^{13}C NMR (151 MHz, DMSO) δ 149.65, 134.72, 129.98, 127.97, 123.90, 116.02. Mp 202–203 °C (lit.[15] 198–202 °C).

4.1.9. 3-(2,4-Dinitrophenyl amino) propionitrile ***(2i)***. Following general procedure, yellow solid (78%, 55.3 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, J=2.5 Hz, 1H), 8.09 (dd, J=9.1, 2.5 Hz, 1H), 6.65 (d, J=9.1 Hz, 1H), 5.33 (s, 1H), 3.69 (q, J=6.4 Hz, 2H), 2.73 (t, J=6.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.47, 138.58, 125.78, 124.69, 118.79, 117.02, 108.76, 39.20, 18.10. HRMS calcd for $C_9H_8N_4O_4$ (M+): 236.0546; found: 236.0545. Mp 134–136 °C (lit.[21e] 134–135 °C).

4.1.10. N-Ethyl-2,4-dinitro-1-naphthylamine ***(2j)***. Following general procedure, yellow solid (81%, 63.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.65 (s, 1H), 9.16 (s, 1H), 8.75 (d, J=8.7 Hz, 1H), 8.32 (d, J=8.5 Hz, 1H), 7.84–7.73 (m, 1H), 7.60–7.54 (m, 1H), 3.98–3.93 (m, 2H), 1.46 (t, J=7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.86, 132.75, 129.92, 128.22, 126.13, 124.93, 124.53, 123.61, 45.94, 16.88. HRMS calcd for $C_{12}H_{11}N_3O_4$ (M+): 261.0750; found: 261.0752. Mp 169–171 °C (lit.[21f] 172 °C).

4.1.11. N-Benzyl-2,4-dinitroaniline ***(2k)***.[16] Following general procedure, yellow solid (84%, 68.9 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 9.15 (d, J=2.6 Hz, 1H), 8.91 (s, 1H), 8.23 (dd, J=9.5, 2.5 Hz, 1H), 7.38 (dt, J=17.6, 7.5 Hz, 5H), 6.91 (d, J=9.5 Hz, 1H), 4.65 (d, J=5.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.16, 136.43, 135.51, 130.33, 129.24, 128.33, 127.03, 124.17, 114.36, 47.54. Mp 114–116 °C (lit.[16] 116 °C).

4.1.12. Bis(2,4-dinitrophenyl)amine ***(2m)***. Following general procedure, pale yellow solid (81%, 84.9 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 11.77 (s, 1H), 9.18 (d, J=2.4 Hz, 2H), 8.46 (dd, J=9.1, 2.4 Hz, 2H), 7.77 (d, J=9.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.00, 140.25, 137.87, 129.63, 123.54, 119.99. HRMS calcd for $C_{12}H_7N_5O_8$ (M+): 349.0295; found: 349.0293. Mp 193–195 °C (lit.[21g] 198 °C).

4.1.13. 2-Methoxy-N-methyl-4,6-dinitroaniline ***(2n)***.[17] Following general procedure, brown-red solid (72%, 49.1 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (d, J=2.5 Hz, 1H), 7.64 (d, J=2.5 Hz, 1H), 3.94 (s, 3H), 3.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.05, 143.30, 135.06, 131.14, 116.80, 108.39, 56.70, 34.08. Mp 217–219 °C (lit.[17] 220–222 °C).

4.1.14. N-Methyl-2,4-dinitroaniline ***(2o)***.[13] Following general procedure, brown-red solid (62%, 36.6 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (d, J=2.6 Hz, 1H), 8.57 (s, 1H), 8.30 (dd, J=9.5, 2.4 Hz, 1H), 6.92 (d, J=9.5 Hz, 1H), 3.15 (d, J=5.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.11, 136.11, 130.41, 124.24, 113.50, 30.24. Mp 172–174 °C (lit.[21a] 175–176 °C).

4.1.15. N,3-Dimethyl-2,4-dinitroaniline ***(2p)***. Following general procedure, pale yellow solid (26%, 16.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, J=9.4 Hz, 1H), 6.68 (d, J=9.4 Hz, 1H), 5.94 (s, 1H), 2.99 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.54, 139.00, 137.32, 131.57, 129.64, 109.41, 30.15, 16.66. HRMS calcd for $C_8H_9N_3O_4$ (M+): 211.0593; found: 211.0595. Mp 80–81 °C (lit.[21h] 81 °C).

4.1.16. N,5-Dimethyl-2,4-dinitroaniline ***(2p′)***.[18] Following general procedure, yellow solid (58%, 36.7 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.37 (s, 1H), 6.67 (s, 1H), 3.11 (d, J=5.1 Hz, 3H), 2.69 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.70, 143.12, 136.81, 129.13, 125.94, 115.83, 30.06 22.44. Mp 170–172 °C (lit.[17] 173 °C).

4.1.17. 5-Cl-N-Methyl-2,4-dinitroaniline ***(2q)***. Following general procedure, yellow solid (65%, 41.7 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.40 (s, 1H), 6.95 (s, 1H), 3.12 (d, J=5.1 Hz, 3H). ^{13}C NMR (151 MHz, DMSO) δ 147.84, 134.39, 133.23, 128.92, 127.08,

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117.16, 30.93. HRMS calcd for $C_7H_6ClN_3O_4$ (M+): 231.0047; found: 231.0044. Mp 163–164 °C (lit.[21i] 161–163 °C).

4.1.18. N-Methyl-2,4-dinitroaniline ***(2s)***.[17] Following general procedure, brown-red solid (50%, 29.5 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 9.15 (d, J=2.6 Hz, 1H), 8.58 (s, 1H), 8.30 (dt, J=15.3, 7.7 Hz, 1H), 6.92 (d, J=9.5 Hz, 1H), 3.15 (d, J=5.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.10, 136.06, 130.42, 124.26, 113.52, 30.25. Mp 173–175 °C (lit.[21a] 175–176 °C).

4.1.19. 2,4-Dinitro-N,N-dimethylaniline ***(4a)***.[19] Following general procedure, yellow solid (86%, 54.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (d, J=2.7 Hz, 1H), 8.20–8.16 (m, 1H), 7.01–6.99 (m, 1H), 3.05 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.08, 136.36, 135.66, 127.70, 124.10, 116.58, 42.37. Mp 174–176 °C (lit.[19] 178 °C).

4.1.20. 1-Piperidinyl-2,4-dinitrobenzene ***(4b)***.[20] Following general procedure, yellow solid (81%, 61.1 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 8.62 (d, J=2.7 Hz, 1H), 8.16 (dd, J=9.4, 2.7 Hz, 1H), 7.07 (d, J=9.4 Hz, 1H), 3.29–3.18 (m, 4H), 1.74–1.63 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.68, 137.16, 127.98, 123.88, 119.05, 51.78, 25.36, 23.44. Mp 90–92 °C (lit.[21j] 91–92.5 °C).

4.1.21. 1-Morpholino-2,4-dinitroaniline ***(4c)***.[12] Following general procedure, brown-red solid (74%, 56.2 mg); ^{1}H NMR (600 MHz, DMSO) δ 8.55 (d, J=2.6 Hz, 1H), 8.23 (dd, J=9.4, 2.7 Hz, 1H), 7.38 (d, J=9.4 Hz, 1H), 3.70–3.68 (m, 4H), 3.26–3.23 (m, 4H). ^{13}C NMR (151 MHz, DMSO) δ 149.22, 137.76, 137.41, 128.61, 123.81, 120.52, 66.06, 50.81. Mp 116–118 °C (lit.[12] 117–118 °C).

4.1.22. 1-(2,4-Dinitrophenyl)–pyrrolidine ***(4d)***. Following general procedure, yellow solid (85%, 60.5 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 8.57 (d, J=2.7 Hz, 1H), 8.11 (dd, J=9.5, 2.7 Hz, 1H), 6.87 (d, J=9.5 Hz, 1H), 3.31 (t, J=6.5 Hz, 4H), 2.06–2.02 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.47, 135.17, 134.69, 127.42, 123.74, 115.48, 51.03, 25.49. HRMS calcd for $C_{10}H_{11}N_3O_4$ (M+): 237.0750; found: 237.0753. Mp 67–69 °C (lit.[21k] 66 °C).

4.1.23. 2,4-Dinitro-N-ethylphenylamine ***(6a)***.[12] Following general procedure, yellow solid (94%, 56.1 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.13 (d, J=2.5 Hz, 1H), 8.49 (s, 1H), 8.26 (dd, J=9.5, 2.4 Hz, 1H), 6.91 (d, J=9.5 Hz, 1H), 3.51–3.42 (m, 2H), 1.42 (t, J=7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.21, 135.89, 130.35, 124.34, 113.82, 38.35, 14.08. Mp 111–112 °C (lit.[12] 112–114 °C).

4.1.24. 5-(Ethylamino)-2,4-dinitrophenol ***(6b)***. Following general procedure, yellow solid (75%, 51.1 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.08 (s, 1H), 9.13 (s, 1H), 8.37 (s, 1H), 6.31 (s, 1H), 3.41–3.35 (m, 2H), 1.41 (t, J=7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.11, 149.81, 127.49, 126.51, 123.75, 98.76, 38.39, 13.78. HRMS calcd for $C_8H_9N_3O_5$ (M+): 227.0542; found: 227.0541. Mp 145–146 °C.

4.1.25. N-Methyl-2,4-dinitroaniline ***(6c)***.[13] Following general procedure, brown-red solid (63%, 37.2 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (d, J=2.6 Hz, 1H), 8.58 (s, 1H), 8.30 (dd, J=9.4, 2.6 Hz, 1H), 6.92 (d, J=9.5 Hz, 1H), 3.15 (d, J=5.2 Hz, 3H). ^{13}C NMR (151 MHz, DMSO) δ 149.21, 135.04, 132.85, 130.36, 123.85, 115.57, 30.74. Mp 172–173 °C (lit.[21l] 175–176 °C).

4.2. Validation experiment of mechanism with *N*-methylaniline

$Bi(NO_3)_3{\cdot}5H_2O$ (2 equiv, 0.6 mmol), $Pd(OAc)_2$ (0.015 mmol, 5 mol %) were added into a 25 mL oven-dried Schlenk tube, the tube was evacuated and backfilled with Ar. Under a counter flow of Ar, *N*-methylaniline (1 equiv, 0.3 mmol) was added by syringe firstly, 1.5 mL TFE and 0.5 mL TFA were then added by disposable medical syringes. The flask was sealed and the mixture was allowed to stir in a preheated oil bath at 90 °C for 1 h. The mixture was cooled to room temperature when the reaction was completed. The solution was diluted by 10 mL ethyl acetate and filtered the insoluble matters, washed the organic phases by distilled water, extracted the aqueous phases by ethyl acetate (3×15 mL) to collect organic phases. All the organic solutions were washed by brine, dried 30 min with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude products were purified by chromatography on silica gel, eluting with ethyl acetate/petroleum ether (25/1).

4.2.1. N-Methyl-2-nitroaniline.[22] Following general procedure, brown-red solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, J=8.6 Hz, 1H), 7.99 (s, 1H), 7.41 (dd, J=8.4, 7.1 Hz, 1H), 6.79 (d, J=8.7 Hz, 1H), 6.59 (dd, J=8.3, 7.2 Hz, 1H), 2.97 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.15, 136.12, 131.61, 126.51, 114.97, 113.21, 29.52. Mp 33–35 °C (lit.[22] 36–37 °C).

4.2.2. N-Methyl-4-nitroaniline.[22] Following general procedure, yellow solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J=8.5 Hz, 2H), 6.52 (d, J=8.5 Hz, 2H), 2.92 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.13, 137.83, 126.35, 110.73, 30.13. Mp 152–153 °C (lit.[22] 149–150 °C).

4.3. General procedures for gram-scale synthesis of *N*-methyl-2,4-dinitroaniline

A 100 mL three-necked round bottom flask was charged with $Bi(NO_3)_3{\cdot}5H_2O$ (20 mmol, 8.1 g) $Pd(OAC)_2$ (5 mol %, 11.3 mg). The tube was evacuated and backfilled with Ar (repeated three times). Under a counter flow of Ar, **1b** (1.1 mL) were added by syringe firstly, and then TFE (45 mL), TFA (15 mL). The flask was sealed and the mixture was stirred firstly at room temperature for 15 min, then allowed to stir in a preheated oil bath at 90 °C for 24 h with condensing. The mixture was cooled to room temperature when the reaction was completed. Next, the organic solvent was washed the organic phases by 5% $NaHCO_3$ solution after the extraction and extracted the aqueous phases by ethyl acetate, dried 30 min with anhydrous $MgSO_4$. The organic solvent was concentrated under reduced pressure. The crude product was purified by chromatography on silica gel with petroleum ether/ethyl acetate to give the product **2b** with the yield of 81%.

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Supplementary data

Supplementary data (Copies of ^{1}H, ^{13}C NMR spectra for the products are available free of charge) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.04.013.

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