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Journal Name

ARTICLE

Construction of 3,5-Dinitrated 1,4-Dihydropyridines Modifiable at 1,4-Positions by a Reaction of β-Formyl-β-nitroenamines with Aldehydes

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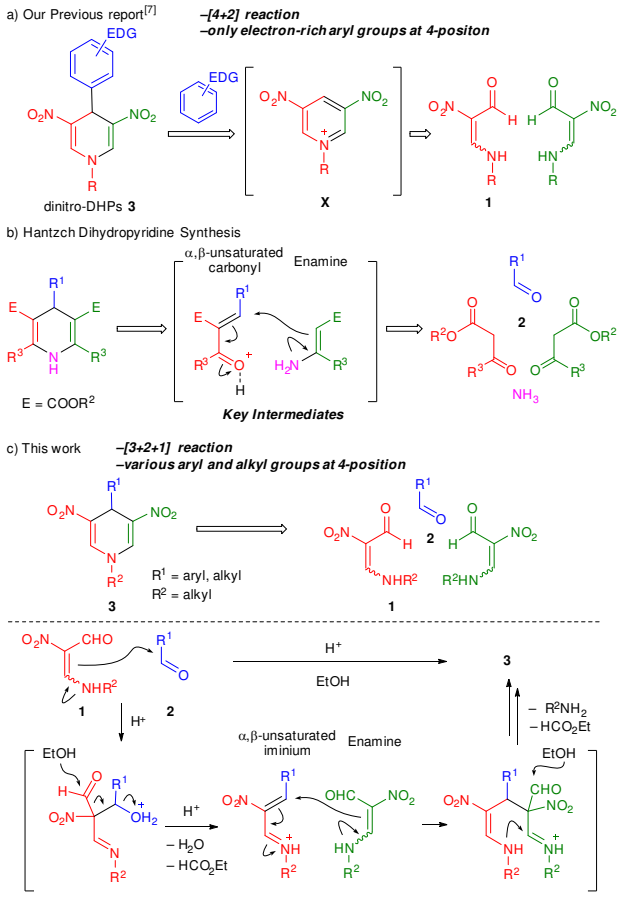
A novel and efficient method for the synthesis of 4-substituted 3,5-dinitro-1,4-dihydropyridines via multi-component reaction of β-formyl-β-nitroenamines with aldehydes was developed. The reaction of nitroenamines with aldehydes leading to 1,4-dihydropyridines and the self-condensation of nitroenamines leading to pyridinium salt intermediate proceed competitively. The obtained 3,4,5-trisubstituted-1,4-dihydropyridines readily transformed into the corresponding pyridines in high yields.

Introduction

1,4-Dihydropyridine (DHP) derivatives have attracted great attention in the medicinal chemistry and pharmacological fields due to their wide spectrum of bioactivities.[1] 4-Arylated DHPs are often found as the fundamental framework in drugs such as calcium antagonists[2] and also the drugs for cardiovascular diseases.[3] Moreover, dimeric DHPs are used as precursors for HIV-1 protease inhibitors.[4] Apart from their medicinal value, DHPs, especially 2,6-unsubstituted DHPs with electron-withdrawing groups at the 3- and 5-positions, have been employed as photoelectronic functional materials.[5] Thus, numerous methods for the preparation of DHPs have been reported. The Hantzsch reaction, a multi-component reaction of an aldehyde, two β-keto esters, and ammonia, is the most widely used.[6] However, only a few cases of the synthesis of 2,6-unsubstituted 3,5-functionalized DHPs have been reported so far; in particular, the introduction of nitro groups at the 3- and 5-positions is quite difficult, mainly because of poor reactivity.

Considering this background, we recently developed a novel method for the construction of 4-arylated 3,5-dinitro-1,4-dihydropyridines (dinitro-DHPs) (Scheme 1(a))[7] by electrophilic substitution of electron-rich benzene derivatives with pyridinium ion **X**, formed by self-condensation of β-formyl-β-nitroenamine **1**. The formylnitroenamine **1** is useful synthetic unit because its versatile reactivity arises from two electrophilic sites, nucleophilic amino group, and electron-



Scheme 1

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Electronic Supplementary Information (ESI) available: Copies of ^{1}H and ^{13}C NMR spectra for new compounds, the details about optimization of reaction conditions, and X-ray crystallographic data (CIF file), ORTEP drawing for **3ab**. See DOI: 10.1039/x0xx00000x

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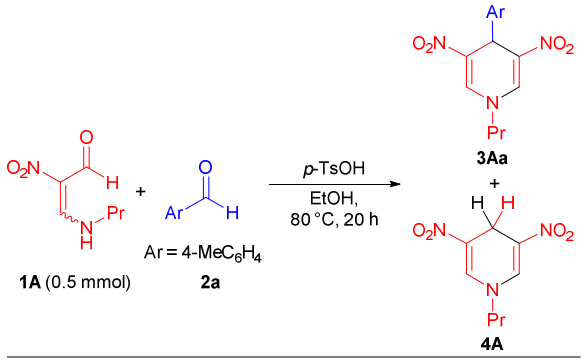
withdrawing nitro group. It is easily prepared from commercially available reagents by a few steps, and they are easily handled because of the high solubility in common organic solvents. Although this reaction affords dinitro-DHPs that are not easily formed by other methods, the substrate scope is limited to highly electron-rich aromatics. Thus, the development of an efficient method for the synthesis of dinitro-DHPs having various groups is highly desirable.

Based on the Hantzsch DHP synthesis,[8] which includes a protonated α,β-unsaturated ketone and an enamine as key intermediates (Scheme 1(b)), a multi-component reaction between two molecules of β-formyl-β-nitroenamine **1** and an aldehyde **2** is designed (Scheme 1(c)). In this strategy, the nitroenamine serves as both an α,β-unsaturated iminium and an enamine, enhancing the synthetic utility of formylnitroenamine as a building block. Herein, we report a new method for the construction of various 4-substituted 3,5-dinitro-1,4-DHPs **3** and their oxidation to afford 3,5-dinitropyridines.

Results and discussion

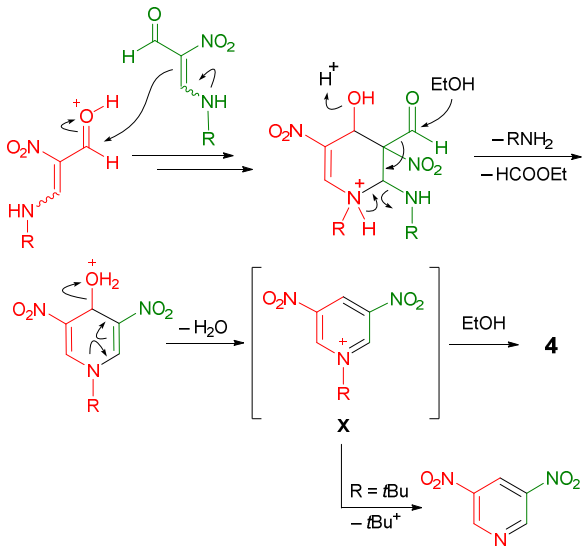
At first, we studied the reaction of *N*-propyl-β-formyl-β-nitroenamine **1A** (0.5 mmol) with *p*-tolualdehyde (Tol-CHO) **2a** under acidic conditions (Table 1). When the reaction was carried out in the presence of *p*-toluenesulfonic acid monohydrate (p-TsOH·H_2O, 0.25 mmol) in ethanol, the desired 4-arylated dinitro-DHP **3Aa** was successfully obtained in 67% yield (entry 1, based on half of **1A**), accompanied by the formation of 4-unsubstituted DHP **4A** (4%). Although the yield of the desired product **3Aa** slightly increased up to 78% when0.5 mmol of *p*-TsOH was used, the yield of the by-product **4A** also increased (entry 2). However, higher amounts

Table 1 Optimization of reaction conditions.



Entry	**2a** (mmol)	*p*-TsOH (mmol)	Yield (%)[a,b]	
			3Aa	**4A**
1	0.5	0.25	67	4
2	0.5	0.5	78	13
3	0.5	1.0	77	12
4	1.0	0.5	84	8
5	2.5	0.5	92 (90)	trace
6	5.0	0.5	77	trace

[a] Determined by ^{1}H NMR. Based on **1A**. [b] Isolated yield was shown in parentheses.

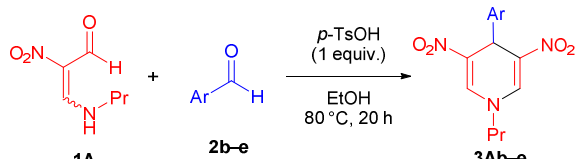


Scheme 2 Proposed mechanism for the formation of 3,5-dinitro-DHPs **4**.

of *p*-TsOH did not significantly affect the reaction (entry 3, for additionaloptimizations see Supporting Information, Table S1). As depicted in Scheme 2, the 4-unsubstituted DHP **4A** was formed by the reduction of the pyridinium ion **X**, which is obtained by self-condensation of **1A** in the absence of aldehyde **2** (more details on the reduction of **X** by alcohol are discussed later).From this viewpoint, increasing the amount of aldehyde was assumed to be effective for suppressing the competitive formation of the by-product **4A**. Accordingly, when 2.5 mmol of **2a** was used, the desired product **3Aa** was successfully isolated in 90% yield with negligible amounts of **4A** (entry 5).

With the optimal conditions being derived, the scope and limitation of this reaction were examined using various aromatic aldehydes **2b–e** (Table 2). In all cases, the desired 4-arylated dinitro-DHPs **3** were obtained in high yields. It is noteworthy that, unlike previous methodologies, electron-neutral (entry 2) and electron-deficient aromatic rings (entries 3 and 4) could be introduced.

Table 2 Scope of the reaction with aromatic aldehydes.



Entry	Ar	Product	Yield (%)[a]
1	4-$MeOC_6H_4$	**3Ab**	84
2	C_6H_5	**3Ac**	84
3	4-ClC_6H_4	**3Ad**	88
4	4-$NO_2C_6H_4$	**3Ae**	80

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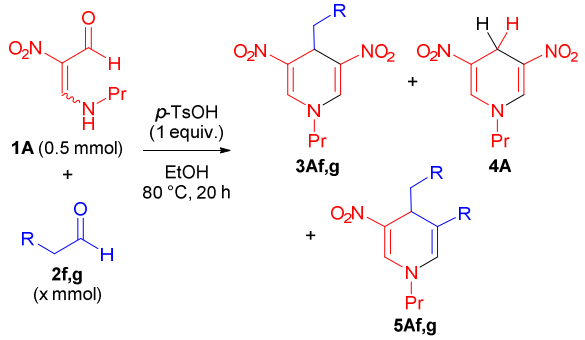
[a] Isolated yield.

Table 3 Scope of the reaction with aliphatic aldehydes.

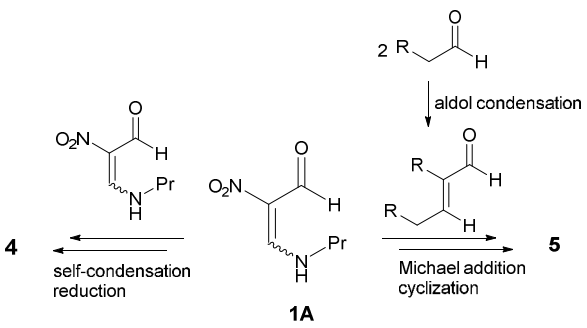


Entry	Aldehyde R	mmol	Yield (%)[a,b] 3	5	4A
1	**2f**: Et	2.5	**3Af** 16	**5Af** 13[c]	5
2	**2f**: Et	0.5	**3Af** 45 (40)	**5Af** 4[c]	19
3	**2g**: *i*Pr	0.5	**3Ag** 71 (70)	**5Ag** trace[c]	13

[a] Determined by ^{1}H NMR. Based on **1A**. [b] Isolated yields were shown in parentheses. [c] Based on aldehyde **2**.

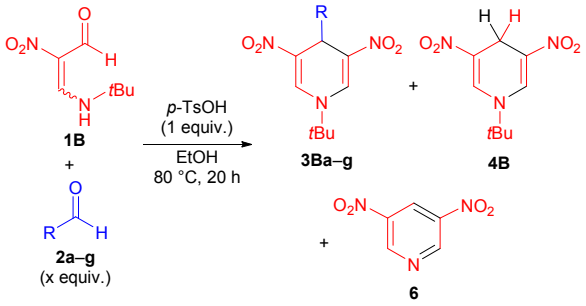
Next, we examined the substrate scope using a more reactive aliphatic aldehyde, i.e., butanal **2f** (Table 3). Although the desired product **3Af** was obtained, the yield was lower than that of 4-arylated DHPs **3Aa–e**, and the 3,4-dialkyl-DHP derivative **5** was also formed (entry 1). Product 5 formed by the Michael addition of the nitroenamine **1A** to the α,β-unsaturated enone that is formed by aldol condensation of butanal **2f** (Scheme 3). This competitive reaction was suppressed by decreasing the amount of aldehyde **2f**, thereby increasing the yield of dinitro-DHP **3Af** up to 45%, accompanied by 19% of unsubstituted product **4A** (entry 2). The undesired aldol reaction of the aldehyde was suppressed by using the bulkier 3-methylbutanal **2g**, which successfully afforded dinitro-DHP **3Ag** in 70% isolated yield (entry 3).

In order to facilitate the modification at the 1-position of the dinitro-DHPs, application of the procedure optimized for **1A** to *N*-*tert*-butyl-β-formyl-β-nitroenamine **1B** was attempted. Nitroenamine **1B** reacted similarly with aromatic aldehydes **2a–e** to afford the corresponding 4-arylated dinitro-DHPs **3Ba–e** in good yields (Table 4, entries 1-5, Figure S1), whereas the reaction with aliphatic aldehydes **2f** and **2g** gave **3Bf** and **3Bg**



Scheme 3 Undesired side reactions.

Table 4 Reaction of *N*-*tert*-butyl-β-formyl-β-nitroenamine **1B** with aldehydes.



Entry	Aldehyde R	mmol	Yield (%)[a] 3	4B	6
1	**2a**: 4-MeOC$_6$H$_4$	2.5	**3Ba** 74	0	24
2	**2b**: 4-MeC$_6$H$_4$	2.5	**3Bb** 60	0	21
3	**2c**: C$_6$H$_5$	2.5	**3Bc** 86	0	14
4	**2d**: 4-ClC$_6$H$_4$	2.5	**3Bd** 81	0	14
5	**2e**: 4-NO$_2$C$_6$H$_4$	2.5	**3Be** 75	0	14
6	**2f**: Propyl	0.5	**3Bf** 26	3	3
7	**2g**: Isobutyl	0.5	**3Bg** 32	0	3
8	—	—	—	3	70

[a] Isolated yield

in low yields (entries 6 and 7). It is noteworthy that, in all cases, 3,5-dinitropyridine **6** was obtained in moderate yields. A plausible mechanism for the formation of **6** is shown in Scheme 2. Upon treatment of **1B** with acid, two molecules of **1B** underwent a formal [4 + 2] condensation to form the pyridinium ion intermediate **XB**, from which the stable *tert*-butyl cation was eliminated to afford the 3,5-dinitropyridine **6**. As expected, **6** was produced in 70% yield when **1B** was treated under the same conditions in the absence of aldehyde **2** (entry 8). The highly electron-deficient heteroarene **6** is a potentially useful and versatile synthetic intermediate;[9] however, its conventionally used preparation method suffers from troublesome multi-step reactions and low total yield.[10] Thus, our reaction using *N*-*tert*-butyl-β-formyl-β-nitroenamine **1B** represents an alternative method for the rapid construction of 3,5-dinitropyridine **6** in high yield.

In this method, in addition to 4-substituted DHPs **3**, 4-unsubstituted DHPs **4** were obtained as by-products. In order to gain an insight into the mechanism of the formation of 4-unsubstituted DHPs **4**, several control experiments were conducted (Scheme 4). When **1A** was treated with TsOH in CD_3CD_2OD (ethanol-d_6), 4-monodeuterated 3,5-dinitro-DHP was obtained in 55% yield along with 10% of 4-CD_3-3,5-dinitro-DHP (Scheme 4(a)). Moreover, when benzyl alcohol was employed as solvent instead of ethanol, 4-phenyl-3,5-dinitro-DHP **3Ac** and 3,5-dinitro-DHP **4** were obtained in 33% and 66% yields, respectively (Scheme 4(b)). In addition, the formation of benzaldehyde was confirmed by the ^{1}H NMR spectrum of the reaction mixture. These observations obviously indicated that the pyridinium ion **X** was reduced by the alcohol via formation of the 4-position alcohol adduct intermediate **Y** (Scheme 5).

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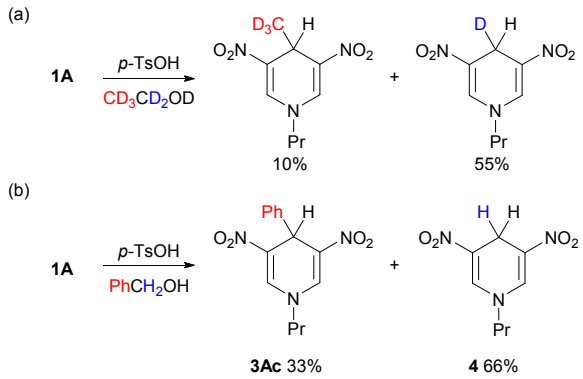
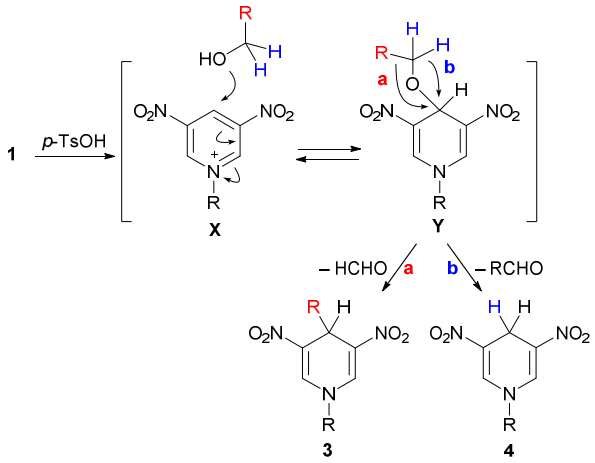


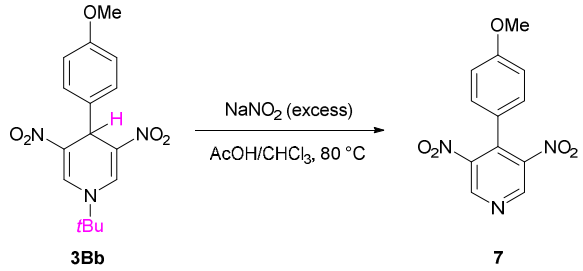
Scheme 4 Control experiments.



Scheme 5 Formation of 3,5-dinitro-DHPs **3** and **4**.

Subsequently, the transfer of the R group leads to 4-substituted products **3** (route a), whereas the intramolecular hydride transfer gives the reduced product **4** (route b). Herein, the reduction of pyridinium ion by alcohol is often found in the biological system, such as NAD^+/NADH system in the presence of dehydrogenase.[11] On the other hand, Lu *et al*. thoroughly studied the mechanism of the reduction of pyridinium ion derivatives by an alcohol in the presence of Brønsted acid and showed the reaction involves intermolecular hydride transfer as transition state similar to biological system.[12] Contrary to these examples, our reaction is first example for the reduction of pyridinium salt by alcohol via intramolecular hydride or alkyl transfer mechanism.

With 4-arylated dinitro-DHPs in hand, we carried out preliminary studies on the oxidative conversion of 4-substituted DHPs to 4-substituted-3,5-dinitropyridines, which are not easily accessible by other methods.[13] As shown in Scheme 6, treatment of 4-anisyl DHP **3Bb** with excess amount of $NaNO_2$ in chloroform under oxygen atmosphere at 80 °C for 24 h to afford the desired product **7** in a promising isolated yield of 68%. The obtained 4-arylated-3,5-dinitropyridines are useful synthetic intermediates for functional materials. Moreover, the push-pull electronic properties of this product



Scheme 6 Oxidation of *N-tert*-butyl-3,5-dinitro-DHP **3Bb**.

are crucial for developing organic materials with potential applications in nonlinear optics.

Conclusions

In conclusion, we have successfully developed a multi-component reaction of β-formyl-β-nitroenamines **1** and aldehydes **2** leading to the formation of diverse 4-substituted 3,5-dinitro-DHPs. This method provides an environmentally benign and metal-free access to a variety of 2,6-unsubstituted 3,5-dinitro-DHPs, which have not been extensively studied because of the synthetic difficulties. From a mechanistic point of view, competitively formed self-condensed pyridinium ion **X** showed interesting reactivity. Namely, alcohols regioselectively attack to 4-position of intermediate **X** to form adduct intermediate **Y**, and then is oxidized via intramolecular hydride or alkyl transfer. This is first example for the reduction of pyridinium salt by alcohol via intramolecular process. In addition, the synthesized DHPs are easily transformed to 4-substituted 3,5-dinitropyridines, which have high potential for nonlinear optical materials. Further applications of the electronic properties of the obtained products in this work are currently underway.

Acknowledgements

We are grateful to Mr. Nobuaki Tsuda (Center for Industry, University and Government Cooperation, Nagasaki University) for the HRMS analysis.

Experimental

General Procedure for the Reaction of *N*-propyl-β-Formyl-β-nitroenamines 1A with p-Tolualdehyde 2a

p-TsOH·H_2O (95 mg, 0.5 mmol) was added to the suspension of β-formyl-β-nitroenamine **1A** (0.5 mmol) and p-tolualdehyde **2a** (306 µL, 2.5 mmol) in ethanol (1 mL), and the resultant mixture was stirred at 80 °C for 20 h in a sealed tube. The solvent was then evaporated in vacuo, and the residue was diluted with CH_2Cl_2 (20 mL) and washed with water (10 mL × 3). After drying ($MgSO_4$) and evaporation of the solvent, the residue

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was purified on silica gel column chromatography (hexane/ethyl acetate = 5/1). Further purification was performed by recrystallization from chloroform. All reactions of nitroenamines with aldehydes were conducted according to general procedure. Compound **3Ab** is known and its spectral data match with reported data.[7]

General Procedure for the Synthesis of 4-Arylated-3,5-Dinitropyridine 7

The oxidation was performed according to literature procedure.[13] To a suspension of 3,5-dinitro-DHP **3Bb** (0.3 mmol, 83 mg) in acetic acid (3 mL) and chloroform (0.5 mL), sodium nitrite (1.5 mmol) was added. The mixture was stirred under oxygen at 80 °C for 24 h in a sealed tube. The mixture was then evaporated, and the residue was diluted with CH_2Cl_2 (20 mL) and washed with water (10 mL × 3). After drying ($MgSO_4$) and evaporation of the solvent, The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 9/1).

1,4-Dihydro-3,5-dinitro-4-(4-methylphenyl)-1-propylpyridine (3Aa)

Orange solid (71.9 mg, 90%): mp 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.07 (t, *J* = 7.2 Hz, 3H), 1.85 (tq, *J* = 7.2, 7.2 Hz, 2H), 2.29 (s, 3H), 3.57 (t, *J* = 7.2 Hz, 2H) 5.61 (s, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.82 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.7 (CH_3), 21.1 (CH), 23.5 (CH_2), 39.3 (CH_3), 57.6 (CH_2), 128.3 (CH), 129.3 (CH), 133.6 (C), 134.6 (CH), 137.5 (C), 137.9 (C); IR (KBr/cm^{-1}) 1672 (C=C), 1489, 1279 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{15}H_{17}N_3O_4$: 303.1219, found 303.1230.

1,4-Dihydro-3,5-dinitro-4-phenyl-1-propylpyridine (3Ac)

Orange solid (60.1 mg, 84%): mp 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.08 (t, *J* = 7.2 Hz, 3H), 1.87 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.58 (t, *J* = 7.2 Hz, 2H) 5.65 (s, 1H), 7.23–7.35 (m, 5H), 7.84 (s, 2H) ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.7 (CH_3), 23.5 (CH_2), 39.7 (CH), 57.6 (CH_2), 128.1 (CH), 128.4 (CH), 128.6 (C), 133.4 (CH), 134.7 (C), 140.3 (C); IR (KBr/cm^{-1}) 1672 (C=C), 1489, 1277 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{14}H_{15}N_3O_4$: 289.1063, found 289.1053.

4-(4-Chlorophenyl)-1,4-dihydro-3,5-dinitro-1-propylpyridine (3Ad)

Orange solid (71.3 mg, 88%): mp 143–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.08 (t, *J* = 7.2 Hz, 3H), 1.88 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.59 (t, *J* = 7.2 Hz, 2H), 5.64 (s, 1H), 7.26–7.28 (m, 4H), 7.84 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.7 (CH_3), 23.5 (CH_2), 39.3 (CH), 57.6 (CH_2), 128.8 (CH), 129.7 (CH), 133.1 (C), 134.1 (CH), 134.9 (C), 138.8 (C); IR (KBr/cm^{-1}) 1674 (C=C), 1489, 1279 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{14}H_{14}ClN_3O_4$: 323.0673, found 323.0670.

1,4-Dihydro-3,5-dinitro-4-(4-nitrophenyl)-1-propylpyridine (3Ae)

Brown oil (66.9 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.09 (t, *J* = 7.2 Hz, 3H), 1.89 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.64 (t, *J* = 7.2 Hz, 2H) 5.77 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.90 (s, 2H), 8.17 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.7 (CH_3), 23.5 (CH_2), 39.9 (CH_3), 57.8 (CH_2), 123.9 (CH), 129.5 (CH), 132.5 (C), 135.5 (CH), 146.9 (C), 147.6 (C); IR (KBr/cm^{-1}) 1681 (C=C), 1506, 1278 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{14}H_{14}N_4O_6$: 334.0913, found 334.0905.

1,4-Dihydro-3,5-dinitro-1,4-dipropylpyridine (3Af)

Brown oil (25.6 mg, 40%); ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.00 (t, *J* = 7.2 Hz, 3H), 1.20 (dt, *J* = 4.4, 7.2 Hz, 2H), 1.64 (tq, *J* = 7.2, 7.2 Hz, 2H),1.76 (tq, *J* = 7.2 , 7.6 Hz, 2H) 3.48 (t, *J* = 7.6 Hz, 2H), 4.79 (t, *J* = 4.4 Hz, 1H), 7.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.6 (CH_3), 13.9 (CH_3), 18.1 (CH_2), 23.5 (CH_2), 33.7 (CH_2), 33.9 (CH), 57.5 (CH_2), 131.9 (C), 136.4 (CH); IR (KBr/cm^{-1}) 1674 (C=C), 1506, 1277 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{11}H_{17}N_3O_4$: 255.1219, found 255.1213.

1,4-Dihydro-3,5-dinitro-4-isobutyl-1-propylpyridine (3Ag)

Brown oil (47.1 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 0.90 (d, *J* = 6.4 Hz, 6H), 1.00 (t, *J* = 7.2 Hz, 3H), 1.46–1.49 (m, 2H), 1.78 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.53 (t, *J* = 7.2 Hz, 2H), 4.78 (dt, *J* = 0.8, 5.2 Hz, 1H), 7.76 (d, *J* = 0.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.6 (CH_3), 23.1 (CH_3), 23.6 (CH_2), 25.1 (CH), 31.8 (CH), 43.9 (CH_2), 57.5 (CH_2), 132.9 (C), 136.1 (CH); IR (KBr/cm^{-1}) 1670 (C=C), 1506, 1277 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{12}H_{19}N_3O_4$: 269.1376, found 269.1385.

1,4-Dihydro-1,4-dipropyl-3-ethyl-5-nitropyridine (5Af)

Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 0.87 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.6 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H), 1.10–1.21 (m, 2H), 1.32–1.45 (m, 1H), 1.60–1.70 (m, 2H), 1.71–1.80 (m, 1H), 2.01–2.22 (m, 2H), 3.23–3.33 (m, 2H), 3.92 (t, *J* = 4.0 Hz, 1H), 5.72 (s, 1H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.8 (CH_3), 11.6 (CH_3), 14.2 (CH_3), 18.0 (CH_2), 23.1 (CH_2), 25.2 (CH_2), 32.9 (CH_2), 36.3 (CH), 56.9 (CH_2), 121.8 (CH), 122.9 (C), 127.8 (C), 140.1 (CH); IR (KBr/cm^{-1}) 1670 (C=C), 1456, 1219 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{13}H_{22}N_2O_2$: 238.1681, found 238.1689.

1,4-Dihydro-4-isobutyl-3-isopropyl-5-nitro-1-propylpyridine (5Ag)

Orange oil; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 0.85 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 7.6 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.21–1.35 (m, 1H), 1.37–1.44 (m, 1H), 1.54–1.73 (m, 3H), 2.38–2.49 (m, 1H), 3.29–3.39 (m, 2H), 3.91 (t, *J* = 4.4 Hz, 1H), 5.72 (s, 1H), 7.87 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 10.8 (CH_3), 20.6 (CH_3), 22.2 (CH_3), 23.1 (CH_3), 23.2 (CH_2), 23.8 (CH_3), 25.3 (CH), 30.2 (CH), 33.5 (CH), 43.9 (CH_2), 57.1 (CH_2), 120.9 (CH), 124.2 (C), 133.4 (C), 139.7 (CH); IR (KBr/cm^{-1}) 1670 (C=C), 1456, 1211 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{15}H_{26}N_2O_2$: 266.1994, found 266.1998.

1-(*tert*-Butyl)-1,4-dihydro-3,5-dinitro-4-(4-methylphenyl)pyridine (3Ba)

Orange solid (58.7 mg, 74%): mp 277–278 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.60 (s, 9H), 2.29 (s, 3H), 5.61 (s,1H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 8.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 21.1 (CH_3), 29.3 (CH_3), 39.3 (CH), 60.3 (C), 128.1 (CH), 129.2 (CH), 131.5 (CH), 133.7 (C), 137.6 (C), 137.8 (C); IR (KBr/cm^{-1}) 1668 (C=C), 1497, 1269 (NO_2). HRMS (ESI, TOF) *m/z* calcd. for $C_{16}H_{20}N_3O_4$ $(M+H)^+$: 318.1454, found 318.1457.

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1-(*tert*-Butyl)-1,4-dihydro-3,5-dinitro-4-(4-methoxyphenyl)pyridine (3Bb)

Orange solid (50.0 mg, 60%): mp 273–274 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.59 (s, 9H), 3.77 (s, 3H), 5.60 (s,1H), 6.82 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 8.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 29.3 (CH_3), 38.9 (CH), 55.3 (CH_3), 60.3 (C), 114.0(CH), 129.4 (CH), 131.4 (CH), 132.8 (C), 133.7 (C), 159.3 (C); IR (KBr/cm^{-1}) 1668 (C=C), 1497, 1269 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{16}H_{19}N_3O_5$: 333.1325, found 333.1315.

1-(*tert*-Butyl)-1,4-dihydro-3,5-dinitro-4-phenylpyridine (3Bc)

Orange solid (65.2 mg, 86%): mp 223–224 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.60 (s, 9H), 5.65 (s,1H), 7.23–7.30 (m, 5H), 8.17 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 29.3 (CH_3), 39.7 (CH), 60.4 (C), 128.0 (CH), 128.3 (CH), 128.6 (CH), 131.7 (CH), 133.6 (C), 140.4 (C); IR (KBr/cm^{-1}) 1670 (C=C), 1487, 1271 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{15}H_{17}N_3O_4$: 303.1219, found 303.1230.

1-(*tert*-Butyl)-4-(4-chlorophenyl)-1,4-dihydro-3,5-dinitropyridine (3Bd)

Orange solid (68.4 mg, 81%): mp 248–249 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.60 (s, 9H), 5.63 (s,1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 8.17 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 29.3 (CH_3), 39.3 (CH), 60.5 (C), 128.8(CH), 129.6 (CH), 131.8 (CH), 133.2 (C), 134.0 (C), 138.9 (C); IR (KBr/cm^{-1}) 1670 (C=C), 1489, 1271 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{15}H_{16}ClN_3O_4$: 337.0829, found 337.0825.

1-(*tert*-Butyl)-1,4-dihydro-3,5-dinitro-4-(4-nitrophenyl)pyridine (3Be)

Brown solid (65.3 mg, 75%): mp 220–221 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 1.62 (s, 9H), 5.77 (s,1H), 7.49 (d, *J* = 8.4 Hz, 2H), 8.17 (d, *J* = 8.4 Hz, 2H), 8.22 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 29.3 (CH_3), 40.0 (CH), 61.0 (C), 123.9 (CH), 129.4 (CH), 132.4 (CH), 132.6 (C), 147.1 (C), 147.6 (C); IR (KBr/cm^{-1}) 1670 (C=C), 1497, 1271 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{15}H_{16}N_4O_6$: 348.1070, found 348.1078.

1-(*tert*-Butyl)-1,4-dihydro-3,5-dinitro-4-propylpyridine (3Bf)

Brown oil (17.6 mg, 26%); ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 0.88 (t, *J* = 4.8 Hz, 3H), 1.18 (tq, *J* = 4.8, 8.5 Hz, 2H), 1.51 (s, 9H), 1.65 (dt, *J* = 4.0, 8.5 Hz, 2H) 4.79 (t, *J* = 4.0 Hz, 1H), 8.10 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 13.9 (CH_3), 17.9 (CH_2), 29.2 (CH_3), 33.6 (CH_3), 33.9 (CH_2), 60.0 (CH), 132.0 (C), 133.2 (C); IR (KBr/cm^{-1}) 1670 (C=C), 1489, 1260 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{12}H_{19}N_3O_4$: 269.1376, found 269.1384.

1-(*tert*-Butyl)-1,4-dihydro-3,5-dinitro-4-isobutylpyridine (3Bg)

Brown oil (22.7 mg, 32%); ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 0.91 (d, *J* = 6.4 Hz, 6H), 1.47–1.48 (m, 3H), 1.52 (s, 9H), 4.78 (t, *J* = 5.2 Hz, 1H), 8.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 23.1 (CH_3), 25.2 (CH), 29.3 (CH_3), 31.8 (CH), 43.6 (CH_2), 60.0 (C), 132.9 (CH), 133.1 (C); IR (KBr/cm^{-1}) 1653 (C=C), 1506, 1271 (NO_2) . HRMS (EI, double focusing) *m/z* calcd. for $C_{13}H_{21}N_3O_4$: 283.1532, found 283.1531.

4-(4-Methoxyphenyl)-3,5-dinitropyridine (7)

Yellow solid (56.1 mg, 68%): mp 139–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C, TMS) δ 3.86 (s, 3H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.19 (d, *J* = 8.8 Hz 2H), 9.15 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 30 °C, TMS) δ 55.4 (CH_3), 114.9 (CH), 119.7 (C), 128.9 (CH), 137.8 (C), 146.6 (C), 146.8 (CH), 161.4 (C); IR (KBr/cm^{-1}) 1539 (C=C), 1360, 1260 (NO_2). HRMS (EI, double focusing) *m/z* calcd. for $C_{12}H_9N_3O_5$: 275.0542, found 275.0538.

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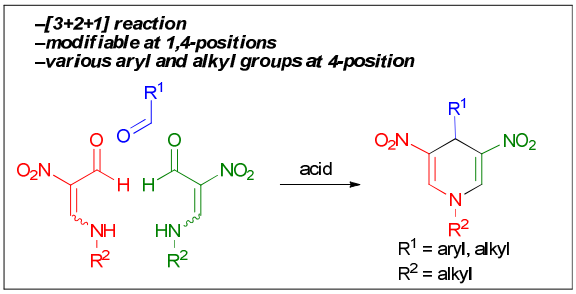

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