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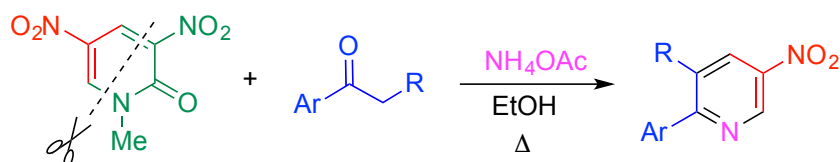
## Synthesis of 2-Aryl-5-nitropyridines by Three Component Ring Transformation of 3,5-Dinitro-2-pyridone

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### Graphical Abstract

#### Synthetic Methods



**Dual ring transformation:** 2-Arylated-5-nitropyridines were efficiently synthesized by a three component ring transformation of 3,5-dinitro-2-pyridone with aromatic ketones in the presence of ammonium acetate. This method was applicable to various kinds of (het)aryl ketones to afford the corresponding (het)arylated pyridines in good to excellent yields.

**Abstract:** 2-Arylated-5-nitropyridines were efficiently synthesized by a three component ring transformation of 3,5-dinitro-2-pyridone with aromatic ketones in the presence of ammonium acetate, in which the dinitropyridone serves as a synthetic equivalent of an unstable nitromalonaldehyde. Although a 2,8-diazabicyclo[3.3.1]non-3-ene derivative was also formed as a by-product, it was converted to nitropyridines under the employed reaction conditions, heating in the presence of ammonium acetate. This experimental fact implies that the former compound is a kinetically controlled product and the latter is thermodynamically controlled product because of the aromatization. This method was applicable to various kinds of aryl and hetaryl ketones to afford the corresponding (het)arylated pyridines in good to excellent yields.

**Keywords**

Biaryls

Multicomponent reactions

Nitrogen heterocycles

Nitropyridines

Ring transformation

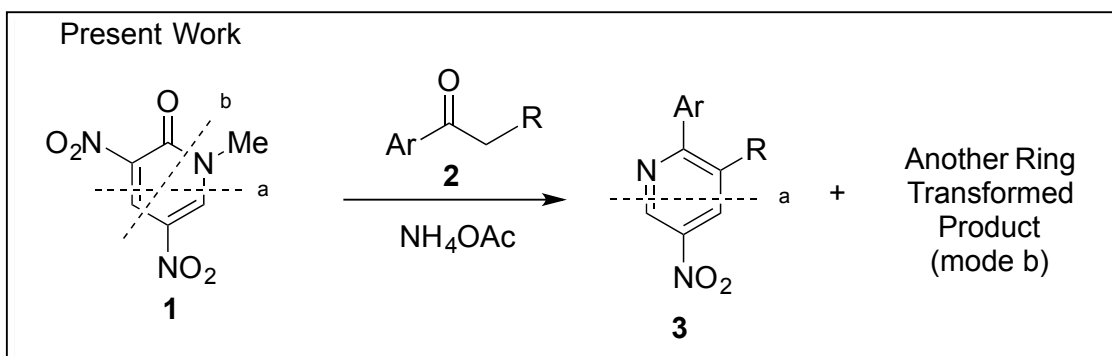
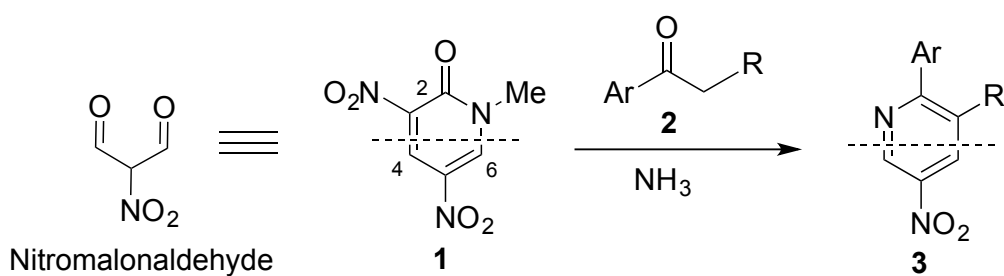
## Introduction

Biaryl frameworks are often found in a variety of natural products and pharmacophores such as vancomycin,<sup>[1]</sup> gossypol,<sup>[1]</sup> shizandrin,<sup>[1]</sup> FHS receptor agonist,<sup>[2]</sup> anti-HIV agent,<sup>[3]</sup> antihypertensive drug,<sup>[4]</sup> antibacterial activity against Gram-positive bacteria<sup>[5]</sup> and so on. While these compounds are widely used for various purposes, arylation of the pyridine frameworks is commonly performed by transition-metal catalyzed coupling reaction using phenylboronic acid (Suzuki reaction) or phenylmagnesium bromide (Kumada-Tamao reaction). However, these methods suffer from availability of functionalized halopyridines and coupling partners.<sup>[6-10]</sup> Especially, electron-deficient aryl groups are not easily introduced to the pyridine framework by these methods, even when severe reaction conditions such as high temperature, long time, and high catalyst loading are used.

Arylated nitropyridines are often used as precursors of biologically active compounds such as Wnt inhibitors,<sup>[11]</sup> inhibitors of stearyl-CoA desaturase,<sup>[12]</sup> bacterial RNAP inhibitors<sup>[13]</sup> drugs for eye diseases and Paget disease,<sup>[9]</sup> and so on. In addition, nitropyridines substituted with an electron-donating aryl group exhibit push-pull property of electrons.<sup>[14]</sup>

Despite these high utilities, it is difficult to prepare arylated nitropyridines by above-mentioned reactions. Hence, development of efficient, easily manipulated and environmentally benign methods for synthesis of arylated nitropyridines remains a significant challenge.

In our previous work, we have represented an alternative preparation method for nitropyridine derivatives by three component ring transformation (TCRT) of 1-methyl-3,5-dinitro-2-pyridone (**1**)<sup>[15,16]</sup> with aromatic ketones in the presence of methanolic ammonia as a nitrogen source (Scheme 1), in which the dinitropyridone **1** serves as a synthetic equivalent of an unstable nitromalonaldehyde.<sup>[17]</sup> Unfortunately, this method requires preparation of methanolic ammonia beforehand, and suffers from low yields of the products because of the competitive ammonolysis of substrate **1**.<sup>[18]</sup> If these disadvantages are overcome, this reaction will be a powerful protocol for synthesis of arylated nitropyridines which are not easily prepared by transition-metal-catalyzed coupling reactions. These circumstances prompted us to study a new ring transformation of dinitropyridone **1** using less nucleophilic ammonium acetate as nitrogen source,<sup>[19]</sup> which avoids the ammonolysis of **1**.



**Scheme 1.** Nucleophilic-type ring transformations of the dinitropyridone **1**

## Results and Discussion

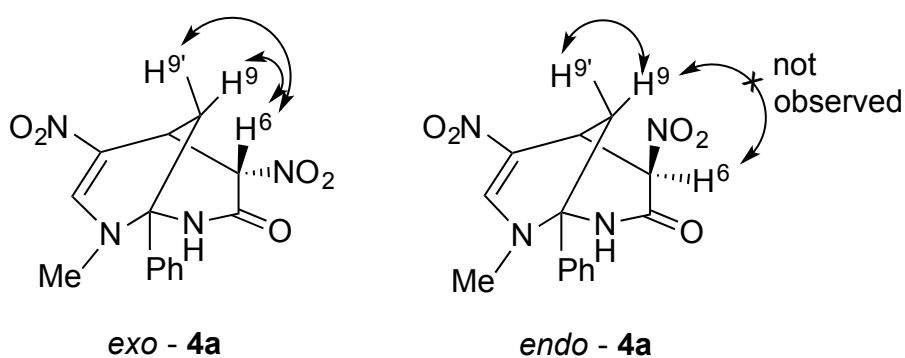
At first, dinitropyridone **1** was allowed to react with acetophenone (**2a**) in the presence of 3 equiv. of ammonium acetate in ethanol for 24 h at 65 °C (Table 1, Entry 1). In this reaction, bicyclic product **4a**<sup>[20]</sup> was isolated in 61% yield besides 19% of 2-phenyl-5-nitropyridine (**3a**).<sup>[6]</sup> In the <sup>1</sup>H NMR spectrum of **4a**, a pair of several signals were observed between 2 and 6 ppm, which indicates that **4a** is a mixture of two non-aromatic stereoisomers. On the basis of spectral and analytical data, the product **4a** was determined to be a 2,8-diazabicyclo[3.3.1]non-3-ene derivative,<sup>[21]</sup> which corresponds to the structure formed by insertion of **2a** and a nitrogen atom between the 1- and 2-positions of the dinitropyridone **1**. The bicyclic structure was finally confirmed by X-ray single crystal analysis using product **4b**, which was derived from 4-nitroacetophenone (**2b**). The isomeric structure was assigned by NOESY spectrum; while both protons H<sup>9</sup> and H<sup>9'</sup> of the *exo*-**4a** showed correlation with H<sup>6</sup>, the correlation between H<sup>9'</sup> and H<sup>6</sup> was not observed in the case of the *endo*-**4a** (Figure 1). The DFT calculations using B3LYP 6-31+G<sup>\*\*</sup> showed the *exo*-**4a** was more stable than the *endo*-**4a** with 3.3 kcal/mol.

**Table 1.** Study on the amount of ammonium acetate affecting the ratio of the products<sup>[a]</sup>

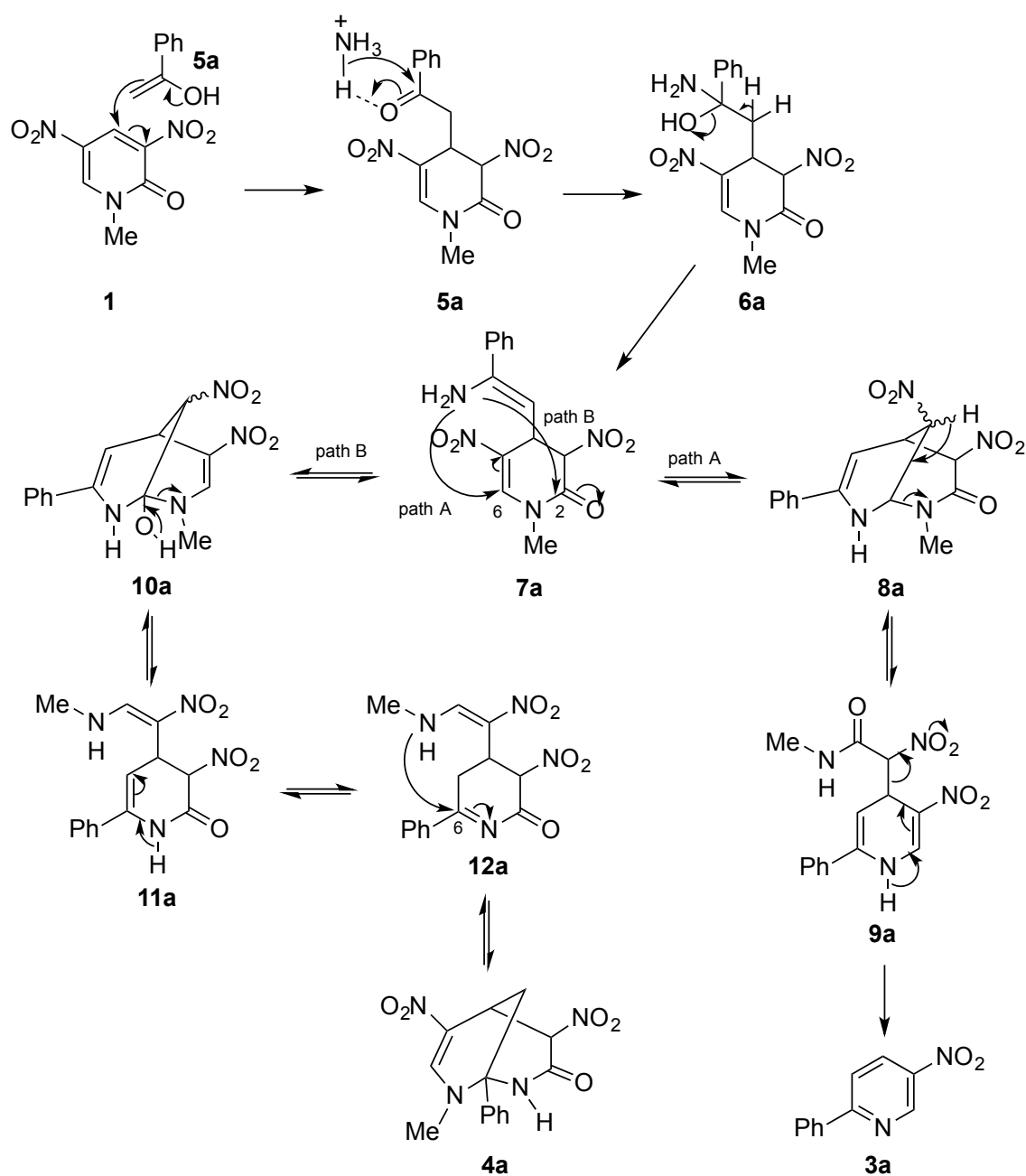
$\text{1 (1 equiv.)} + \text{2a (1 equiv.)} \xrightarrow[\text{EtOH}]{\text{NH}_4\text{OAc, 65 }^\circ\text{C}}$ 
 $\text{3a} + \text{4a}$

Entry	NH <sub>4</sub> OAc [equiv.]	Time [h]	Yield [%] <sup>[b]</sup>			Ratio of 3a/4a	Ratio of <i>exo</i> -4a/ <i>endo</i> -4a
			3a	4a	3a+4a		
1	3	24	19	61	80	24/76	56/44
2	5	24	43	46	89	48/52	59/41
3	10	24	64	25	89	72/28	70/30
4	15	24	79	0	79	100/0	—
5	15	16	75	8	83	90/10	25/75
6	15	8	61	14	75	81/19	46/54
7 <sup>[c]</sup>	5	7	92	5	97	95/5	60/40
8 <sup>[c]</sup>	15	5	90	0	90	100/0	—

[a] All reactions were performed using 0.25 mmol (50 mg) of **1** and 0.25 mmol (29.5  $\mu$ l) of **2a**. [b] Yield of products **3a** and **4a** after simple extraction with chloroform. [c] Microwave heating was used.



**Figure 1.** Correlations between H<sup>6</sup> and H<sup>9</sup>, H<sup>9'</sup> of the isomers **4a** in the NOESY spectra



**Scheme 2.** A plausible mechanism for the formation of products **3a** and **4**

A plausible mechanism for the formation of the products **3a** and **4a** is illustrated in Scheme 2. The reaction is initiated by the addition of the ketone **2a** in an enol form at the 4-position of the dinitropyridone **1** giving the adduct, benzoylmethylpyridone **5a**, which is then converted to the enaminopyridone **7a** as a result of the reaction with an ammonium ion. The enamine **7a** serves as a common

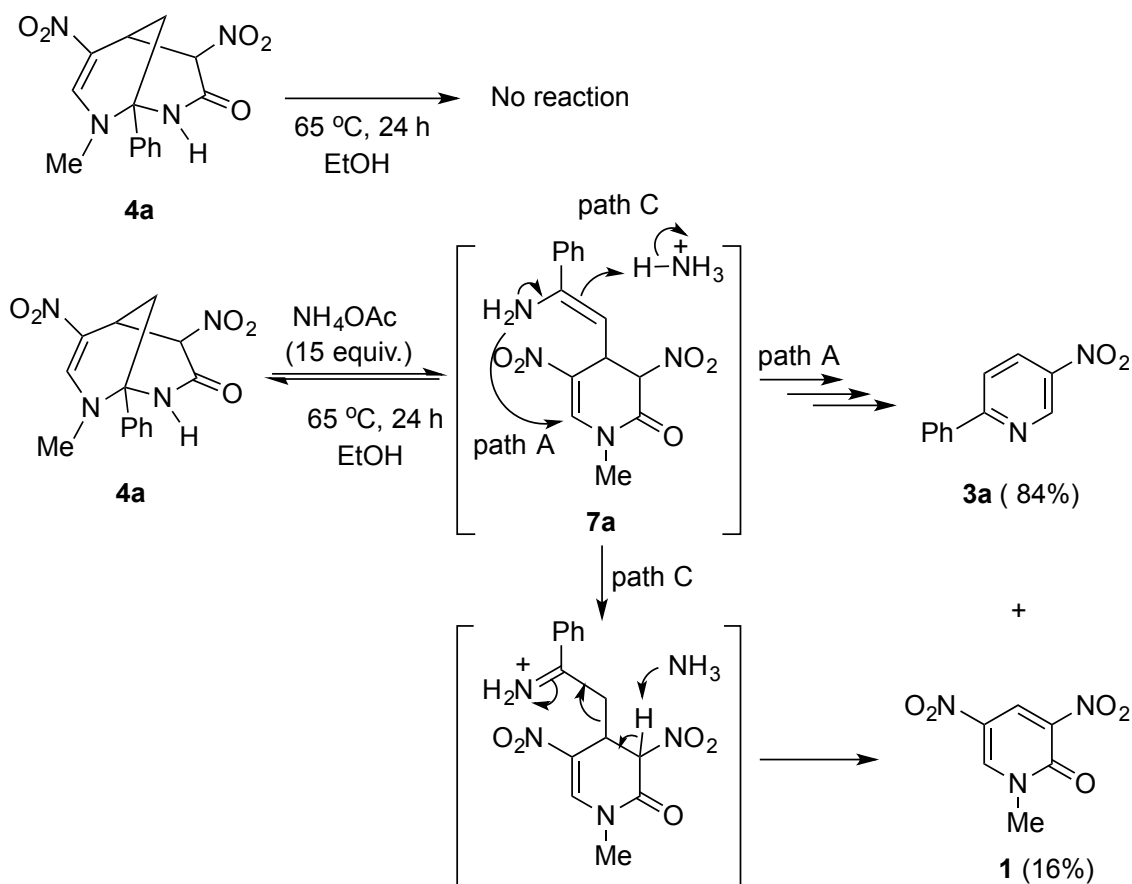
intermediate for both products **3a** and **4a**. When the amino group of **7a** attacks at the 6-position (mode a in Scheme 1, path A in Scheme 2), the nitropyridine **3a** is produced by the formation of the bicyclic intermediate **8a**, which undergoes the ring opening reaction and the aromatization accompanied by the elimination of nitroacetamide.<sup>[15]</sup>

On the other hand, when the amino group of **7a** attacks the carbonyl group at the 2-position (mode b in Scheme 1, path B in Scheme 2),<sup>[15,22]</sup> the bicyclic intermediate **10a** is formed. Since its bridgehead carbons are connected with three hetero atoms, the ring opening reaction easily proceeds leading to the intermediate **11a**. Then, the amino group attacks the 6-position of the tautomer **12a** to afford bicyclic product **4a**.

The selectivity between paths A and B was considerably affected by the amount of ammonium acetate. The nitropyridine **3a** was obtained in only 19% yield, when 3 equiv. of ammonium acetate was used (Table 1, entry 1). The yield of **3a** increased up to 79% accompanied by decreasing in the yield of bicyclic product **4a** with largely increasing the amount of ammonium acetate (entries 2-4).

When the reaction time was shortened, the ratio of **3a/4a** decreased although the total yields were almost similar (entries 4-6). This result indicated that the bicyclic product **4a** was converted to **3a** upon heating the reaction mixture for a longer time. In addition, microwave heating was found to be more effective than conventional heating, which considerably reduced the reaction time and increased the yield of **3a** (entries 7 and 8). As showed in Table 1, the conversion from **4a** to **3a** possibly proceeded under severe conditions. While the bicyclic product **3a** was intact in an ethanol solution at 65 °C, it was converted to the aromatized nitropyridine **3a** and dinitropyridone **1**, in 84% and 16%, respectively, in the presence of ammonium acetate (Scheme 3, paths A and C). This result indicates that there is an equilibrium between **4a** and **7a**.

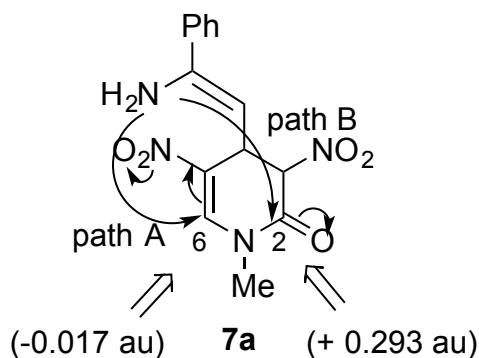




**Scheme 3.** Conversion of the bicyclic compound **4a** to nitropyridine **3a** and dinitropyridone **1**

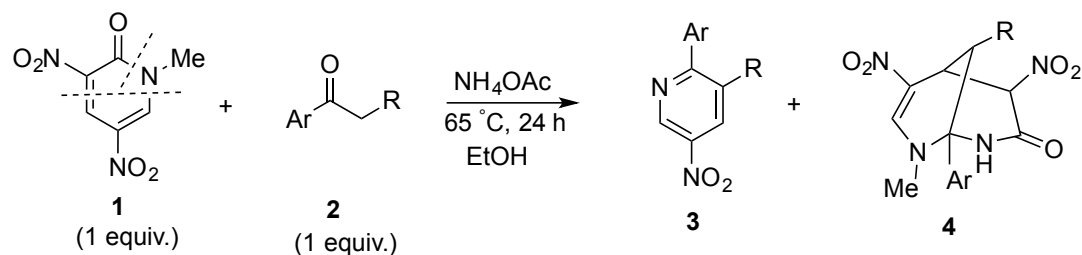
The Mülliken population of the enaminopyridone **7a** determined by DFT calculations revealed that the 2-position is electron-deficient to be attacked by the amino group easily (Figure 2). Thus, the bicyclic product **4a** is predominantly formed via path B in the earlier stage of the reaction; the bicyclic product **4a** is a kinetically controlled product. When the reaction mixture is heated for a longer time, the bicyclic product **4a** is converted to the dinitropyridone **1** via the intermediate **7a** under equilibrium, leading to the stable aromatic product **3a** via path A; the product **3a** is a thermodynamically controlled product. In the present TCRT, competitive thermal decomposition of ammonium acetate also proceeded, and ammonia gas went away from the reaction mixture. When all ammonium acetate were consumed by the TCRT or the decomposition, the TCRT could not proceed anymore because of lacking a nitrogen

source. Hence, further increasing the amount of ammonium acetate prolongs real reaction time, which consequently increased the yield of the nitropyridine **3a**.



**Figure 2.** Mülliken population of the enaminopyridone **7a** determined by DFT calculations (DFT B3LYP/6-31+G\*\*)

The yield of nitropyridines **3** was not only affected by the amount of ammonium acetate but also affected by electron property of the substituent. Therefore, other substituted acetophenones were employed to study the influence of the electronic property of the ketones **2** for the present TCRT (Table 2). The acetophenones **2c** and **2d** having a strong electron-donating methoxy group at the 4- and 2-position revealed high reactivity to afford the corresponding nitropyridines **3c** and **3d** in high yields without the detectable bicyclic product **4c** and **4d** (entries 3 and 4). In the case of 3-methoxyacetophenone (**2e**), the yield of the nitropyridine **3e** decreased because the 3-methoxy group behaves as an electron-withdrawing group for the carbonyl group by an inductive effect, which prevents the approach to the electron-deficient dinitropyridone **1**. The efficiency of the reaction was improved by increasing the amount of ammonium acetate (entries 5 and 6). 4-Methylacetophenone and 4-chloroacetophenones (**2f** and **2g**) also underwent the TCRT to furnish the corresponding nitropyridines **3f** and **3g** in high yields, respectively (entries 7-9). In the case of the electron poor 4-nitroacetophenone (**2b**), the nitropyridine **3b** was efficiently formed in 93% yield by using 15 equiv. of ammonium acetate (entries 10 and 11).

**Table 2.** Ring transformation with other aromatic ketones **2**<sup>[a]</sup>

Entry	Ar	R	NH <sub>4</sub> OAc [equiv.]	Yield [%]			Ref. for <b>3</b> <sup>[c]</sup>	
				<b>3</b> <sup>[c]</sup>	<b>4</b>	<b>3+4</b>		
1	Ph	H	<b>a</b>	5	43	46	89	[6,9,15b]
2	Ph	H	<b>a</b>	15	79	0	79	
3 <sup>[d][e]</sup>	4-MeOC <sub>6</sub> H <sub>4</sub>	H	<b>c</b>	5	95	0	95	[8,9,15b]
4	2-MeOC <sub>6</sub> H <sub>4</sub>	H	<b>d</b>	5	94	0	94	[9,10]
5	3-MeOC <sub>6</sub> H <sub>4</sub>	H	<b>e</b>	5	74	0	74	[9,16b]
6	3-MeOC <sub>6</sub> H <sub>4</sub>	H	<b>e</b>	10	97	0	97	
7	4-MeC <sub>6</sub> H <sub>4</sub>	H	<b>f</b>	5	88	0	88	[9,15b,23]
8	4-ClC <sub>6</sub> H <sub>4</sub>	H	<b>g</b>	5	84	0	84	[9]
9	4-ClC <sub>6</sub> H <sub>4</sub>	H	<b>g</b>	10	96	0	96	
10	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	<b>b</b>	5	42	15	57	[15b,24]
11	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	<b>b</b>	15	93	2	95	
12	4-Pyridyl	H	<b>h</b>	15	66	33	99	[25]
13	3-Pyridyl	H	<b>i</b>	15	97	0	97	[9]
14	2-Pyridyl	H	<b>j</b>	15	80	12	92	[15b,26]
15	2-Furyl	H	<b>k</b>	5	87	0	87	[15b,27]
16	2-Thieryl	H	<b>l</b>	10	85	0	85	[9,15b]
17	2-Prrolyl	H	<b>m</b>	10	87	0	87	[16b]
18	Ph	Me	<b>n</b>	15	31	0	31	[15b,28]
19 <sup>[d][f]</sup>	Ph	Me	<b>n</b>	15	98	0	98	
20	Ph	Pr	<b>o</b>	15	34	0	34	
21 <sup>b,d</sup>	Ph	Pr	<b>o</b>	15	97	0	97	

[a] All reactions were performed using 0.25 mmol (50 mg) of **1** and 0.25 mmol of **2**. [b] Yield of products **3** and **4** after simple extraction with chloroform. [c] All nitropyridines except for **3o** are known compounds. [d] Microwave heating was used. [e] For 6 h. [f] at 80 °C for 2 h.

The present TCRT was applied to the heterocyclic ketones **2h-m** to afford bihetaryl compounds **3h-m**. While the reaction of the dinitropyridone **1** with 3-acetylpyridine (**2i**) afforded the pyridylpyridine **3i** exclusively, considerable amounts of the bicyclic products **4h** and **4j** were obtained, when the more electron-deficient ketones **2h** and **2j** were employed (entries 12-14). To the contrary, the electron-rich ketones **2k- m** showed high reactivity leading to **3k-m** in good yields, respectively (entries 15-17).

## Conclusion

In summary, we have successfully developed a highly efficient and general methodology for synthesis of 2-aryl-5-nitropyridines **3** in good to excellent yields using three component ring transformation reaction of the dinitropyridone **1** with the aromatic ketones **2** in the presence of ammonium acetate. In this reaction, the bicyclic product **4** was isolated and the ratio of the nitropyridine **3** and the bicyclic product **4** was found to be affected by the amount of ammonium acetate. Furthermore, the bicyclic product **4** was converted to the nitropyridine **3** via the dinitropyridone **1** under equilibrium.

From environmental and economic points of view, the present TCRT has great advantages. This method requires only simple manipulations, mild conditions during both the reaction and work-up. Especially, solid ammonium acetate is an easily treatable nitrogen source than gaseous ammonia and unreacted ammonium acetate is easily removed from the reaction mixture by thermal decomposition even when an excess amount of ammonium acetate is used. Furthermore, this method is transition metal free, which enables to omit a purification step for removal of the poisonous transition metal contamination.

This method also facilitates to modify the 2- and 3-positions of the nitropyridines **3** by only changing the ketones **2**, which affords nitropyridines having either an electron-rich or an electron-poor (het)aryl group on demand. Hence, the present ring transformation provides a new methodology for the synthesis of various kinds of (het)arylated nitropyridines, which are not easily prepared by alternative methods.

## Experimental Section

### *General*

The melting points were determined on a Yanaco micro-melting-points apparatus, and were uncorrected. The dinitropyridone **1** was synthesized according to literature procedures.<sup>[29]</sup> All the reagents and solvents were commercially available and used as received. The <sup>1</sup>H NMR spectra were measured on a Bruker Ascend-400 at 400 MHz with TMS as an internal standard. The <sup>13</sup>C NMR spectra were measured on a Bruker Ascend-400 at 100 MHz, and assignments of <sup>13</sup>C NMR spectra were performed by DEPT experiments. The IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. The mass spectra and the high resolution mass spectra were measured on a JEOL JMS-DX303HF.

### *Crystal Structure Determination*

X-ray diffraction data were collected on a Rigaku AFC7R diffractometer with graphite monochromatized Mo-K $\alpha$  radiation. Unit cell parameters were determined by least-squares refinement of 22 automatically centered reflections. The data were corrected for Lorentz and polarization effects. Direct methods (SIR-2008) were used to determine the structure.<sup>[30]</sup> All calculations were performed using the CrystalStructure<sup>[31]</sup> crystallographic software package except for refinement, which was performed using SHELXL-97<sup>[32]</sup>. Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in their idealized positions and refined as rigid atoms with the relative isotropic displacement parameters. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no.CCDC-976536. Copies of the data can be obtained free of charge on application to CCDC, 12 UnionRoad, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

### *General procedure of TCRT*

To a solution of the nitropyridone **1** (50 mg, 0.25 mmol) in ethanol (5 mL), were added acetophenone (**2a**) (29  $\mu$ L, 0.25 mmol) and ammonium acetate (96.3 mg, 1.25 mmol), and then the resultant mixture was heated at 65 °C for 24 h. After removal of the solvent, the residue was washed with benzene (3  $\times$  10 mL) to remove unreacted ketone **2a**, which affords a mixture of the nitropyridine **3a** and the bicyclic product **4a**. The mixture

was extracted with chloroform (3 × 10 mL) to give almost pure nitropyridine **3a** (21.5 mg, 0.12 mmol, 43%) from the organic layer, the bicyclic product **4a** was obtained as a residue (34.2 mg, 0.12 mmol, 46%). It is noted that all ammonium acetate were consumed or competitively decomposed during reaction. The TCRT reaction of the dinitropyridone **1** with other ketones was performed in a similar way.

*2,8-Diaza-2-methyl-4,6-dinitro-7-oxo-1-phenyl-bicyclo[3.3.1]nona-3-ene (4a)*

Yellow powder; mp 227–228 °C (dec.). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 2.23-2.46 (m, 2H<sub>endo</sub>+2H<sub>exo</sub>), 2.89 (s, 3H<sub>endo</sub>+3H<sub>exo</sub>), 2.86 (s, 3H<sub>endo</sub>+3H<sub>exo</sub>), 3.96-4.18 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 5.30 (s, 1H<sub>endo</sub>), 6.01 (d, *J* = 5.2 Hz, 1H<sub>exo</sub>), 7.43-7.51 (m, 5H<sub>endo</sub>+5H<sub>exo</sub>), 8.47 (s, 1H<sub>endo</sub>), 8.55 (s, 1H<sub>exo</sub>), 9.91 (s, 1H<sub>endo</sub>+1H<sub>exo</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) *exo*-isomer: δ 31.9 (CH), 35.0 (CH<sub>2</sub>), 38.9 (CH<sub>3</sub>), 72.2 (C), 87.2 (CH), 120.0 (C), 125.9 (CH), 128.9 (CH), 129.0 (CH), 147.6 (CH), 163.4 (C) (one signal was not observed due to overlapping); *endo*-isomer: δ 31.0 (CH), 32.5 (CH<sub>2</sub>), 38.2 (CH<sub>3</sub>), 71.8 (C), 84.4 (CH), 119.1 (C), 125.8 (CH), 128.8 (CH), 129.0 (CH), 146.6 (CH), 161.5 (C) (one signal was not observed due to overlapping); MS (EI) *m/z* 318 (M<sup>+</sup>, 3), 216 (100), 199 (42), 115 (46), 104 (49), 77 (54); IR (KBr, cm<sup>-1</sup>): 1357, 1558, 1608, 1702, 3459; HRMS (EI, magnetic field) Calcd for C<sub>14</sub>H<sub>14</sub>N<sub>4</sub>O<sub>5</sub>: 318.0964. Found: 318.0965.

*2,8-Diaza-2-methyl-4,6-dinitro-1-(4-nitrophenyl)-7-oxo-bicyclo[3.3.1]nona-3-ene (4b)*

Yellow powder (14 mg, 0.38 mmol, Yield 15%); mp 185–187 °C (dec.). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 2.23-2.44 (m, 2H<sub>endo</sub>+2H<sub>exo</sub>), 2.90 (s, 3H<sub>endo</sub>+3H<sub>exo</sub>), 4.02-4.22 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 5.35 (s, 1H<sub>endo</sub>), 6.02 (d, *J* = 4.8 Hz, 1H<sub>exo</sub>), 7.75 (d, *J* = 8.8 Hz, 1H<sub>endo</sub>), 7.76 (d, *J* = 8.8 Hz, 1H<sub>exo</sub>), 8.34 (d, *J* = 8.8 Hz, 1H<sub>endo</sub>), 8.35 (d, *J* = 8.8 Hz, 1H<sub>exo</sub>), 8.47 (s, 1H<sub>endo</sub>), 8.56 (s, 1H<sub>exo</sub>), 10.1-10.2 (br, 1H<sub>endo</sub>+1H<sub>exo</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) *exo*-isomer δ 31.8 (CH), 32.3 (CH<sub>2</sub>), 34.7 (CH<sub>3</sub>), 72.1 (C), 87.1 (CH), 120.0 (2C), 125.9 (CH), 128.9 (CH), 129.0 (CH), 147.6 (CH), 163.4 (C); *endo*-isomer δ 31.0 (CH), 32.5 (CH<sub>2</sub>), 38.2 (CH<sub>3</sub>), 71.8 (C), 84.2 (CH), 119.6 (2C), 124.0 (CH), 127.8 (CH), 146.5 (CH), 147.7 (C), 161.5 (C); MS (EI) *m/z* 261 (100), 199 (67), 164 (55), 149 (50), 102 (57); IR (KBr, cm<sup>-1</sup>) 1349, 1558, 1616, 1693, 3444; HRMS (EI, magnetic field) Calcd for C<sub>14</sub>H<sub>13</sub>N<sub>5</sub>O<sub>7</sub>: 363.0815. Found: 363.0813.

*2,8-Diaza-2-methyl-4,6-dinitro-7-oxo-1-(4-pyridyl)bicyclo[3.3.1]nona-3-ene (4h)*

Yellow powder (26 mg, 0.083 mmol, Yield 33%); mp 232–233 °C (dec.). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 2.23-2.44 (m, 2H<sub>endo</sub>+2H<sub>exo</sub>), 2.90 (s, 3H<sub>endo</sub>+3H<sub>exo</sub>), 4.02-4.24 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 5.34 (s, 1H<sub>endo</sub>), 6.01 (d, *J* = 5.2 Hz, 1H<sub>exo</sub>), 7.46 (dd, *J* = 1.6, 6.4 Hz, 2H<sub>endo</sub>), 7.51 (dd, *J* = 1.6, 6.4 Hz, 2H<sub>exo</sub>), 8.48 (s, 1H<sub>endo</sub>), 8.56 (s, 1H<sub>exo</sub>), 8.71-8.74 (m, 2H<sub>endo</sub>+2H<sub>exo</sub>), 9.93-10.11 (br, 1H<sub>endo</sub>+1H<sub>exo</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) *exo*-isomer δ 31.7 (CH), 34.4 (CH<sub>2</sub>), 37.9 (CH<sub>3</sub>), 71.1 (C), 87.1 (CH), 120.4 (C), 121.0 (CH), 146.5 (C), 147.4 (CH), 150.5 (CH), 163.5 (C); *endo*-isomer: δ 30.9 (CH), 32.0 (CH<sub>2</sub>), 37.2 (CH<sub>3</sub>), 71.3 (C), 84.3 (CH), 119.5 (C), 120.9 (CH), 145.9 (C), 147.4 (CH), 150.4 (CH), 161.5 (C); IR (KBr, cm<sup>-1</sup>) 1280, 1558, 1612, 1700, 3457; HRMS (EI, magnetic field) Calcd for C<sub>13</sub>H<sub>13</sub>N<sub>5</sub>O<sub>5</sub>: 319.0917. Found: 319.0915.

*2,8-Diaza-2-methyl-4,6-dinitro-7-oxo-1-(2-pyridyl)bicyclo[3.3.1]nona-3-ene (4j)*

Yellow powder (10 mg, 0.03 mmol, Yield 12%); mp 228–230 °C (dec.). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 2.24-2.40 (m, 2H<sub>endo</sub>+2H<sub>exo</sub>), 2.85 (s, 3H<sub>endo</sub>), 2.86 (s, 3H<sub>exo</sub>), 4.02-4.04 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 4.22-4.25 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 5.33 (s, 1H<sub>endo</sub>), 6.01 (d, *J* = 5.2 Hz, 1H<sub>exo</sub>), 7.51-7.53 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 7.64-7.72 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 7.98-8.04 (m, 1H<sub>endo</sub>+1H<sub>exo</sub>), 8.48 (s, 1H<sub>endo</sub>), 8.56 (s, 1H<sub>exo</sub>), 8.68-8.87 (m, H<sub>endo</sub>+H<sub>exo</sub>), 9.67-9.82 (br, 1H<sub>endo</sub>+1H<sub>exo</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) *exo*-isomer δ 30.9 (CH), 33.0 (CH<sub>2</sub>), 38.4 (CH<sub>3</sub>), 72.3 (C), 87.3 (CH), 120.3 (C), 121.4 (CH), 124.4 (CH), 138.1 (CH), 147.2 (CH), 149.1 (C), 149.4 (CH), 163.5 (C); *endo*-isomer δ 30.6 (CH), 31.7 (CH<sub>2</sub>), 38.1 (CH<sub>3</sub>), 72.0 (C), 84.4 (CH), 121.3 (C), 121.4 (CH), 124.4 (CH), 137.9 (CH), 146.3 (CH), 149.0 (C), 149.3 (CH), 161.5 (C); IR (KBr, cm<sup>-1</sup>) 1307, 1580, 1612, 1675, 3465; HRMS (EI, magnetic field) Calcd for C<sub>13</sub>H<sub>13</sub>N<sub>5</sub>O<sub>5</sub>: 319.0917. Found: 319.0919.

*2-Phenyl-3-propyl-5-nitropyridine (3o)*

Yellow powder (58 mg, 0.24 mmol, Yield 97%); mp 90–92 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 0.87 (t, *J* = 7.2, 14.4 Hz, 3H), 1.65 (tq, *J* = 7.6, 15.6 Hz, 2H), 2.75 (t, *J* = 7.6, 15.6 Hz, 2H), 7.48-7.51 (m, 5H), 8.40 (d, *J* = 2.6 Hz, 1H), 9.32 (d, *J* = 2.6 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 13.75 (CH<sub>3</sub>), 23.67 (CH<sub>2</sub>), 34.33 (CH<sub>2</sub>), 128.46 (CH), 128.70 (CH), 129.10 (CH), 131.93 (CH), 136.77 (CH), 138.88 (C), 141.90 (C), 143.11 (C), 164.44 (CH); IR (KBr, cm<sup>-1</sup>) 1346, 1571; HRMS (EI, magnetic field) Calcd for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>: 242.1055. Found: 242.1052.

### *Conversion of the bicyclic product 4a to the nitropyridine 3a and the dinitropyridone 1*

To a solution of the bicyclic product **4a** (30 mg, 0.09 mmol) in ethanol (5 mL), was added ammonium acetate (289 mg, 3.75 mmol), and the mixture was heated at 65 °C for 24 h. After removal of solvent, the residue was extracted with chloroform (10 mL × 3) to give a mixture of the nitropyridine **3a** (15 mg, 0.075 mmol, 84%) and the dinitropyridone **1** (2.8 mg, 0.014 mmol, 16%).

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