

Construction of 3,5-Dinitrated 1,4-Dihydropyridines Modifiable at 1,4-Positions via Multicomponent Reaction of β -Formyl- β -nitroenamine

Haruyasu Asahara,^{*ab} Mai Hamada,^a Yumi Nakaike,^{a†} and Nagatoshi Nishiwaki^{*ab}

School of Environmental Science and Engineering, Kochi University of Technology, Kami, Kochi 782-8502, Japan.

E-mail: nishiwaki.nagatoshi@kochi-tech.ac.jp; asahara.haruyasu@kochi-tech.ac.jp

Research Center for Material Science and Engineering, Kochi University of Technology,

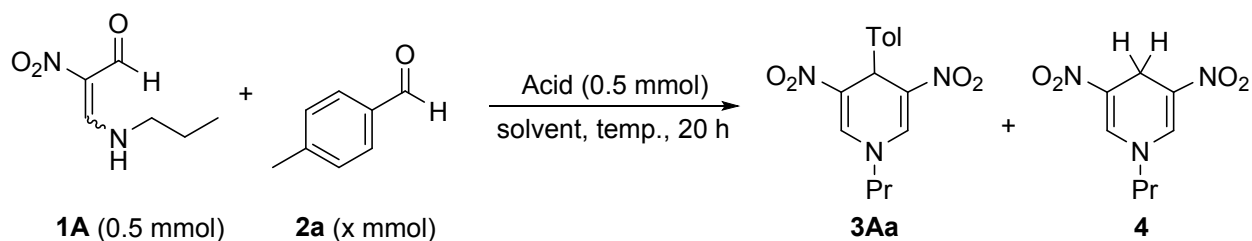
Contents

1. Optimization of Reaction Conditions	S2
2. X-ray Crystal Structure of Compound 3Ba	S3
3. Copies of ¹ H and ¹³ C NMR Spectra for New Compounds	S4

1. Optimization of Reaction Conditions

The results were shown as blow.

Table S1. Evaluation of reaction conditions



Entry	Solvent	Acid	Temp. (°C)	2a (mmol)	Yield (%) ^[a]	
					3	4
1	Neat	<i>p</i> -TsOH	80	0.5	61	trace
2	PhH	<i>p</i> -TsOH	80	0.5	56	0
3	MeCN	<i>p</i> -TsOH	80	0.5	59	trace
4	H ₂ O	<i>p</i> -TsOH	80	0.5	55	0
5	MeOH	<i>p</i> -TsOH	80	0.5	75	trace
6	EtOH	<i>p</i> -TsOH	80	0.5	78	13
7	<i>i</i> -PrOH	<i>p</i> -TsOH	80	0.5	73	trace
8	HFIP ^[b]	<i>p</i> -TsOH	80	0.5	45	0
9	EtOH	HCl	80	0.5	77	7
10	EtOH	BF ₃ ·OEt ₂	80	0.5	60	21
11	EtOH	none	80	0.5	0	0
12	EtOH	<i>p</i> -TsOH	rt	0.5	36	0
13	EtOH	<i>p</i> -TsOH	120	0.5	79	trace
14	EtOH	<i>p</i>-TsOH	80	2.5	92	trace

^[a] Determined by ¹H NMR. Based on the amount of **1A** used. ^[b] (CF₃)₂CHOH

2. X-ray Crystal Structure of Compound 3Ba

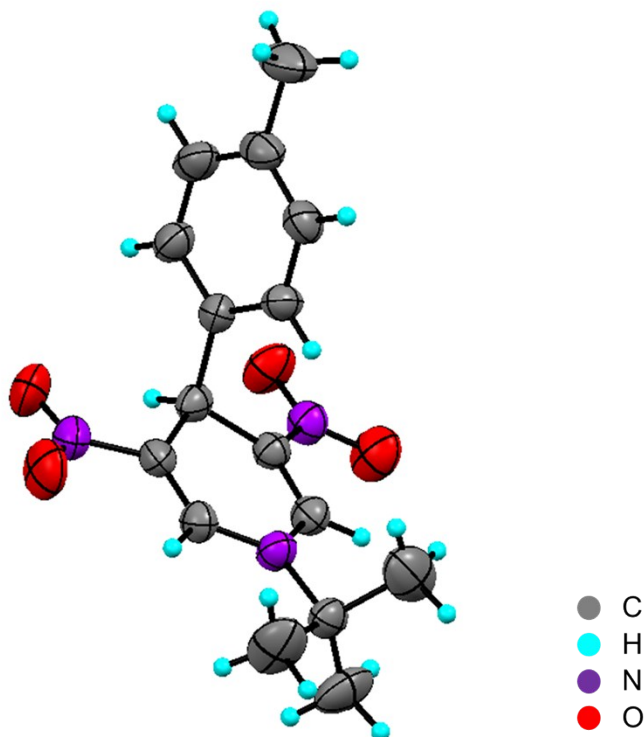


Figure S1. ORTEP showing the *N*-tert-butyl 3,5-dinitro-DHP **3Ba** (Color labels: gray, carbon; cyan, hydrogen; violet, nitrogen; red, oxygen). Within the crystal structure, one *tert*-butyl group is disordered over two orientations, with occupancies of 0.639 (12) and 0.361 (12) (one orientation is removed for clarity).

Thermal ellipsoids are drawn at the 50% probability level. CCDC # 1416840.

X-ray Structure Determination. The crystal data for **3Ba** was collected and integrated with graphite monochromated Mo-K α ($\lambda = 0.71069$ Å) radiation at 296 K. The structure was solved by direct methods^[S1] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement^[S2] on F^2 was based on 3628 observed reflections and 236 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R_1 = \sum ||F_o| - |F_c|| / \sum |F_o| = 0.0737$$

$$wR_2 = [\sum (w (F_o^2 - F_c^2)^2) / \sum w(F_o^2)^2]^{1/2} = 0.2878$$

The standard deviation of an observation of unit weight^[S3] was 0.97. Unit weights were used. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.25 and -0.24 e / Å³, respectively.

Neutral atom scattering factors were taken from Cromer and Waber^[S4]. Anomalous dispersion effects were included in F_{calc} ^[S5]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley^[S6]. The values for the mass attenuation coefficients are those of Creagh and Hubbell^[S7]. All calculations were performed using the

CrystalStructure^[S8] crystallographic software package except for refinement, which was performed using SHELXL-97^[S9]. Crystal data for **3Ba**: CCDC: 1416840, C₁₆H₁₉N₃O₄, M_r = 317.34, monoclinic space group *P*2₁/*c*, a = 8.798(4) Å, b = 10.031(5) Å, c = 17.925(4) Å, β = 94.20(3) °, V = 1577.8(11) Å³, Z = 4, ρ_{calcd} = 1.336 g·cm⁻³, μ = 0.974 cm⁻¹, F(000) = 672, R₁ = 0.0737, wR₂ = 0.2878, 3628 independent reflections [2θ ≤ 50°] and 236 parameters.

References

[S1] SIR2008: M.C. Burla, R. Caliendo, M. Camalli, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori, D. Siliqi, R. Spagna (2007)

[S2] Least Squares function minimized: (SHELXL97)

$$S_w(F_o^2 - F_c^2)^2 \quad \text{where } w = \text{Least Squares weights.}$$

[S3] Standard deviation of an observation of unit weight:

$$[S_w(F_o^2 - F_c^2)^2 / (N_o - N_v)]^{1/2}$$

where: N_o = number of observations

N_v = number of variables

[S4] Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

[S5] Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964).

[S6] Creagh, D. C. & McAuley, W.J. ; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

[S7] Creagh, D. C. & Hubbell, J.H.; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

[S8] CrystalStructure 4.0: Crystal Structure Analysis Package, Rigaku Corporation (2000-2010). Tokyo 196-8666, Japan.

[S9] SHELXL97: Sheldrick, G.M. (2008). Acta Cryst. A64, 112–122.

3. Copies of ^1H and ^{13}C NMR Spectra for New Compounds

