Reaction of Nitric Oxide with Amines

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Reactions of nitric oxide (NO) with amines in organic solvents were studied using Hantzsch dihydropyridines and aromatic primary amines as substrates. Hantzsch dihydropyridines are readily oxidized by nitric oxide to give the corresponding pyridines in quantitative yields. The addition of oxygen accelerates the reaction rate considerably. On the other hand, aromatic primary amines give deaminated products by the reaction with nitric oxide only in the presence of oxygen in ethereal solvents or chloroform.

Because of the well-recognized importance of nitric oxide (NO),[1] many papers have been presented concerning biological and cytotoxic roles of NO. Studies on the chemical reactivity of NO were also begun only recently. The reported reactions can be divided into two categories, those using NO under oxygen atmosphere[2] and others[3] that are performed only with NO in the presence or absence of an inert gas.[4] Recently, we reported two reactions of NO with amino compounds that involve Hantzsch dihydropyridines[5] and aromatic primary amines[6] as substrates in organic solvents. The reaction was clarified with respect to the influence of oxygen, and it was found that a catalytic amount of oxygen affected these two reactions in different manners. This paper describes these results.

The oxidation of Hantzsch 1,4-dihydropyridines **1** is an old reaction in general organic chemistry. Even in recent years, several groups have reported new methods for aromatization including oxidations with ferric or cupric nitrates on a solid support,[7] ceric ammonium nitrate,[8] clay-supported cupric nitrate accompanied by ultrasound-promotion,[9] or pyridinium chlorochromate.[10] There has also been a general method using nitric acid,[11] although all these reactions require different workup procedures. In our experiments, we found that NO oxidized Hantzsch dihydropyridines to give the corresponding pyridine derivatives in quantitative yields.

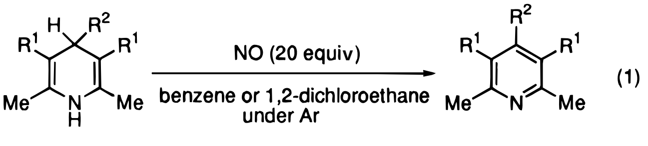
Table 1. Aromatization of Hantzsch Dihydropyridines 1 with Nitric Oxide under Ar Atmosphere

entry	substrate	R^1	R^2	condns	product	yield (%)
1	**1a**	CO_2Et	H	benzene, rt, 3 h	**2a**	96
2				$ClCH_2CH_2Cl$, rt, 3 h		99
3	**1b**	CO_2Et	Me	benzene, rt, 4.5 h	**2b**	96
4				$ClCH_2CH_2Cl$, rt, 2.5 h		97
5	**1c**	CO_2Et	Et	benzene, rt, 3 h	**2c**	96
6				$ClCH_2CH_2Cl$, rt, 1 h		97
7	**1d**	CO_2Et	Pr	benzene, rt, 3 h	**2d**	95
8				$ClCH_2CH_2Cl$, rt, 3 h		100
9	**1e**	CO_2Et	3-CH[a]	benzene, rt, 2 h	**2e (2a)**	34 (47)[b]
10				$ClCH_2CH_2Cl$, rt, 1 h		29 (67)
11	**1f**	CO_2Et	Ph	benzene, rt, 3 h	**2f**	96
12				$ClCH_2CH_2Cl$, rt, 5.5 h		92
13	**1g**	CN	i-Pr	$ClCH_2CH_2Cl$, rt, 1 h	**2g**	99
14	**1h**	CN	3-CH[a]	$ClCH_2CH_2Cl$, rt, 2 h	**2h**	92

[a] 3-Cyclohexenyl is abbreviated as 3-CH. [b] In the case of **1e**, **2a** was obtained in 47% (in benzene) and 67% (in $ClCH_2CH_2Cl$) yields other than **2e**.

Results and Discussion

Reaction of Hantzsch 1,4-Dihydropyridines with NO. Compound **1** was dissolved in benzene or 1,2-dichloroethane under Ar atmosphere, and NO was introduced to the reaction system with a gas-tight syringe (eq 1). After the consumption of the starting material, the solvent was evaporated to leave almost pure product except in the case of **1e** (Table 1).



1 **2** (1)

Substrate **1e** was transformed to a mixture of 4-(3-cyclohexenyl)pyridine **2e** and 4H-pyridine **2a**, which were separated by silica gel chromatography. Substrates **1g** and **1h** have poor solubilities in benzene; thus, the reaction was performed only in 1,2-dichloroethane solution (Table 1, entries 13 and 14). The influence of oxygen on the reaction yield was investigated using **1a** as a

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[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1997.

[1] *Methods in Nitric Oxide Research*; Feelisch, M., Stamler, J. S., Ed.; John Wiley &Sons: Chichester, 1996.

[2] (a) de la Breteche, M.-L.; Servy, C.; Lenfant, M.; Ducrocq, C. *Tetrahedron Lett.* **1994**, *35*, 7231. (b) Nagano, T.; Takizawa, H.; Hirobe, M. *Tetrahedron Lett.* **1995**, *36*, 8239. (c) d'Ischia, M. *Tetrahedron Lett.* **1995**, *36*, 8881. (d) d'Ischia, M. *Tetrahedron Lett.* **1996**, *37*, 5773.

[3] (a) Korth, H.-G.; Ingold, K. U.; Sustmann, R.; de Groot, H.; Sies, H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 891. (b) Wilcox, A. L.; Janzen, *E. G. J. Chem. Soc., Chem. Commun.* **1993**, 1377. (c) Janzen, E. G.; Wilcox, A. L.; Manoharan, V. *J. Org. Chem.* **1993**, *58*, 3597. (d) Freeman, F.; Huang, B.-G.; Lin, R. I.-S. *J. Org. Chem.* **1994**, *59*, 3227. (e) Mukaiyama, T.; Hata, E.; Yamada, T. *Chem. Lett.* **1995**, 505. (f) Hata, E.; Yamada, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 3629.

[4] Pryor *et al.* reported that a small amount of oxygen changes the reactivity of NO toward thiols: (a) Pryor, W. A.; Church, D. F.; Govindan, C. K.; Crank, G. *J. Org. Chem.* **1982**, *47*, 156. Related papers were published recently; see: (b) Kharitonov, V. G.; Sundquist, A. R.; Sharma, V. S. *J. Biol. Chem.* **1995**, *270*, 28158. (c) Goldstein, S.; Czapski, G. *J. Am. Chem. Soc.* **1996**, *118*, 3419. There have been some reports that suggest that minute quantities of O_2, which was not added to the reaction mixtures deliberately, might bring about reactions of substrates with NO; see: (d) Challis, B. C.; Kyrtopoulos, S. A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 299. (e) Afzal, M.; Walton, J. C. *BioMed. Chem. Lett.* **1996**, *6*, 2329.

[5] Itoh, T.; Nagata, K.; Okada, M.; Ohsawa, A. *Tetrahedron Lett.* **1995**, *36*, 2269.

[6] Itoh, T.; Matsuya, Y.; Nagata, K.; Ohsawa, A. *Tetrahedron Lett.* **1996**, *37*, 4165.

[7] Balogh, M.; Hermecz, I.; Meszaros, Z.; Laszlo, P. *Helv. Chim. Acta* **1984**, *67*, 2270.

[8] Pfister, J. R. *Synthesis* **1990**, 689.

[9] Maquestiau, A.; Mayence, A.; Eynde, J.-J. V. *Tetrahedron Lett.* **1991**, *32*, 3839.

[10] Eynde, J.-J. V.; Mayence, A.; Maquestiau, A. *Tetrahedron* **1992**, *48*, 463.

[11] Böcker, R. H.; Guengerich, F. P. *J. Med. Chem.* **1986**, *29*, 1596.

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Table 2. Effect of Oxygen on the Reaction Yield of 2a[a]

entry	amount of O_2 (μL)	ratio of O_2/NO	yield of **2a** (%)
1	0	0	39
2	5	0.0002	56
3	12.5	0.0005	66
4	20	0.0008	100

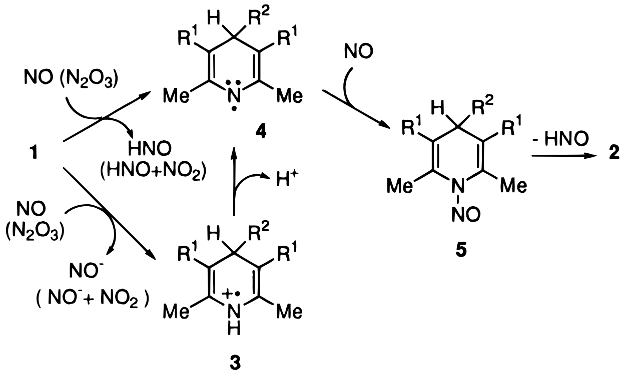
[a] The reaction of **1a** was carried out with 10 equiv of NO in dichloroethane for 2 h.

Table 3. Influence of the Solvent on the Reaction of 1a with NO (20 equiv) under Ar[a]

solvent	yield of **2a** (%)	solvent	yield of **2a** (%)
benzene	96	CH_3CN	91
DCE	99	CH_3OH	20
$CHCl_3$	94	THF	18

[a] The reaction time is 3 h for all the reactions.

Scheme 1



substrate. The results obtained show that a trace amount of oxygen highly accelerates the reaction rate (Table 2, entries 2−4).

It is well known that NO rapidly reacts with O_2 to give nitrogen dioxide NO_2, and NO_2 thus formed is transformed to nitrous anhydride N_2O_3 in the presence of excess NO.[12] Therefore, the acceleration shown above is probably due to the higher reactivity of N_2O_3 (or NO_2) than that of NO; N_2O_3 (or NO_2) is supposed to react with **1** in a catalytic fashion. Provided that O_2 added to the reaction system is transformed to N_2O_3 (or NO_2) stoichiometrically, the reactivity of N_2O_3 (or NO_2) toward **1a** may be about 10^3 times higher[13] than that of NO.[14]

The investigation of solvent effects (Table 3) shows that basic solvents give poor reaction yields, which is in accord with the results reported previously for the reaction of NO with alkenes.[3e,f]

The presumed reaction mechanism is shown in Scheme 1. The reaction might commence with a hydrogen abstraction from the NH group in dihydropyridine[15] or one-electron transfer from **1** to NO to give the ammoniumyl radical **3**, and both paths lead to an aminyl radical **4**. A radical coupling of **4** with NO might form *N*-nitroso derivative **5**, which eliminates HNO to afford the aromatized product. In the case of N_2O_3 as an oxidant, it seems reasonable that N_2O_3 should react with **1** in catalytic fashion. Thus, the reaction of **1** with N_2O_3 might release NO_2, which regenerates another N_2O_3 by the reaction with excess NO.

Table 4. Aromatization of Hantzsch Dihydropyridines 1 with Nitric Oxide under O_2 Atmosphere

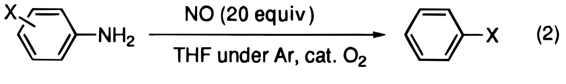
entry	substrate	amount of NO (equiv to **1**)	condns	product	yield (%)
1	**1a**	0.2	benzene rt, under O_2, 10 min	**2a**	98
2	**1b**	0.6		**2b**	84
3	**1c**	0.7		**2c**	89
4	**1d**	0.6		**2d**	97
5	**1e**	0.5		**2e (2a)**	0 (97)[a]
6	**1f**	0.7		**2f**	95
7	**1a**	0.001	benzene, rt, under O_2, 7 days	**2a**	93

[a] In the case of **1e**, **2a** was obtained as a sole product.

Other nitrogen oxides are also reactive toward Hantzsch dihydropyridines. Thus, **1a** was aromatized with 1 equiv of NO under Ar to give 94% of **2a** after 44 h reaction. The stoichiometry of the reaction suggests that HNO (or NO^-) might also react with **1a**, although the reaction mechanism remains unclear.

The use of a smaller amount of NO completed the reaction in a similar manner when excess O_2 was used (see Table 4). There is, however, one noticeable difference between the results of Tables 1 and 4. Namely, substrate **1e** afforded **2a** as a sole product under O_2 atmosphere (Table 4, entry 5), while it gave a mixture of **2a** and **2e** under Ar (Table 1, entries 9 and 10). In this system, an active species might be NO_2, which oxidizes **1** accompanied by the formation of NO, and NO thus obtained is reoxidized to NO_2 by excess O_2.[16]

Reaction of Aromatic Primary Amines with Nitric Oxide in the Presence of a Catalytic Amount of Oxygen. The above results prompted us to initiate an investigation of the reactivity of nitric oxide with other amines. Although aromatic primary amines were reported to react with NO in the presence of excess O_2 to afford triazene derivatives in benzene solution,[2b] it was found that the same substrates reacted with NO in the presence of a catalytic amount of O_2 to give deaminated products in ethereal solvents or chloroform.[6] Our previous communication[6] did not include any information about the influence of oxygen. Further investigations revealed that ca. 0.000 05 equiv of O_2 in NO was crucial for the reaction progress (1 μL of O_2 in 22.4 mL of NO). The reaction proceeded in moderate to high yields except for aromatic amines, which have an electron-donating group in their *meta* position (eq 2 and Table 5).[17]



6 7

The reaction produced a transient precipitate, which slowly dissolved in the solvent to afford the deaminated product. When the precipitate in THF was isolated and dissolved in water followed by the addition of *N*,*N*-

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[12] Von Gratzel, M.; Taniguchi, S.; Henglein, A. *Ber. Bunsenges. Phys. Chem.* **1970**, *74*, 488.

[13] For example, in the case of entry 2 in Table 2, N_2O_3 might be formed at 1/2500 of NO, and the reaction yield was 1.435 times higher than that in the absence of oxygen. Thus, the reactivity of N_2O_3 might be 1087 times higher (0.435 × 2500) than that of NO. The calculations using data of Table 2, entries 3 and 4, give the values 692 and 978, respectively.

[14] Korth *et al.* reported that NO_2 reacts at least 200 times as rapidly as NO with 7,7,8,8-tetramethyl-*o*-quinodimethane: Korth, H.-G.; Sustman, R.; Lommes, P.; Ernst, A.; de Groot, H.; Hughes, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1994**, *116*, 2767. The result is in agreement in the order of magnitude with our estimation.

[15] When **1** was methylated at N-1, it was inert to this reaction. Thus, we supposed that an initial hydrogen abstraction might not occur at the C-4 position.

[16] The organic reactions using NO_2 and excess dioxygen were throughly investigated by Kochi *et al.* including detailed reaction mechanisms; see: Bosch, E; Kochi, J. K. *J. Am. Chem. Soc.* **1996**, *118*, 1319 and references cited therein.

Table 5. Deamination of Aromatic Amines 6 with NO in THF under Ar Atmosphere with a Catalytic Amount of O_2

entry	substrate	X	time (h)	product	yield (%)
1	**6a**	H	2	**7a**	86[a]
2	**6b**	*o*-SMe	6	**7b**	71
3	**6c**	*m*-SMe	24	**7c**	20
4	**6d**	*p*-SMe	2	**7d**	74
5	**6e**	*o*-Cl	5	**7e**	88[a]
6	**6f**	*m*-Cl	3	**7f**	87[a]
7	**6g**	*p*-Cl	3	**7g**	82[a]
8	**6h**	*o*-NO_2	2	**7h**	93
9	**6i**	*m*-NO_2	2	**7i**	78
10	**6j**	*p*-NO_2	2	**7j**	90
11	**6k**[b]	*o*-OMe	5	**7k**	55
12	**6l**[b]	*m*-OMe	24	**7l**	trace
13	**6m**[b]	*p*-OMe	7	**7m**	64

[a] Determined by HPLC analysis. Other yields were obtained from the NMR data. [b] The reactions were carried out in the presence of 2 μL of O_2. The other experiments were with 1 μL of O_2.

Scheme 2

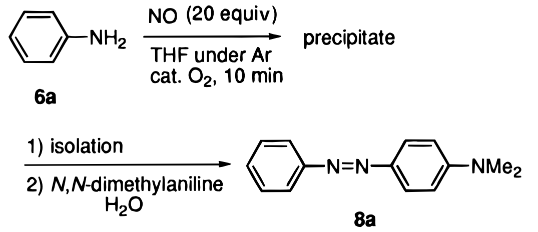
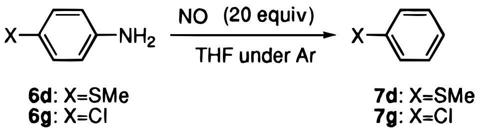


Table 6. Influence of Oxygen on the Reaction Yields of 7

entry	substrate	amount of O_2 (equiv to NO)	yield of **7** (%)	recovery of **6** (%)
1	**6d**	0	trace	0
2	**6d**	0.000 05	82	0
3	**6g**	0	8	68
4	**6g**	0.000 05	82	0
5	**6g**	0.005	91	0
6	**6g**	0.05	86	0
7	**6g**	0.5	66	0

dimethylaniline, an azo product **8a**[18] was obtained (Scheme 2). This result indicates that the deaminated product is formed *via* the intermediacy of a diazonium salt.[19]

Influence of O_2 on the reaction yields was studied using **6d** (X = *p*-SMe) and **6g** (X = *p*-Cl) as substrates, and the results are summarized in Table 6 (eq 3). Even without the addition of O_2, consumption of **6** was observed (Table 6, entries 1 and 3). Compound **6d**, which has an electron-donating group, was consumed more completely than **6g**. Thus, the first step is suggested to involve an oxidative process that is accelerated by an electron-donating substituent. In contrast, the deaminated products were obtained in higher yields when an electron-withdrawing substituent exists on the aniline ring (Table 5), which indicates that the second step involves a reductive process that requires a trace amount of oxygen.



(3)

Table 7. Solvent Effects on the Deamination of (Methylthio)aniline (6d) Using NO in the Presence of a Catalytic Amount of Oxygen[a]

solvent	yield of **7d** (%)	solvent	yield of **7d** (%)
THF	82	benzene	trace[e]
$CHCl_3$	80	CH_3CN	22
DME[b]	81	$CDCl_3$	56[f]
DCE[c]	43[d]		

[a] The reaction time is 2 h except in the case of $CDCl_3$ (24 h). [b] 1,2-Dimethoxyethane. [c] 1,2-Dichloroethane. [d] In addition to **7d**, trace amount of methyl phenyl sulfoxide was detected. [e] 4-(Methylthio)biphenyl was obtained in 28% yield. [f] *p*-Deuteriated **7d** was obtained as a sole product.

Table 8. Influence of NO Amount on the Reaction Yields

substrate	amount of NO (equiv)	reaction time (h)	yield of **7** (%)
6g	3	96	87
6g	2	144	35
6d	3	96	66

The effect of solvent was examined for the deamination of **6d** (Table 7). Ethereal solvents and chloroform afforded good results. On the other hand, 1,2-dichloroethane and benzene, which were used for the reaction of **1**, and previously reported solvents for the reaction of NO,[2b,3e,f] were less effective in the deamination. In benzene solution, 4-(methylthio)biphenyl was obtained in 28% yield as a side product. When $CDCl_3$ was used for the solvent, the reaction proceeded more slowly than with $CHCl_3$, and the product isolated was *p*-deuteriothioanisole. The results show that hydrogen abstraction from the solvent ($CHCl_3$) is required to form the deaminated product. Thus, a phenyl radical was suggested to be one of the intermediates of the reaction.

In addition, when the reaction of **6d** was carried out in carbon tetrachloride, 4-chlorothioanisole was obtained in 52% yield. Moreover, in the presence of diphenyl disulfide in benzene, compound **6d** afforded 1-(methylthio)-4-(phenylthio)benzene in 29% yield along with 38% of 4-(methylthio)biphenyl. These facts also support the intermediacy of a phenyl radical.

In order to estimate the stoichiometry, the reaction was carried out using a decreased amount of NO in the presence of oxygen. It was necessary to lengthen the reaction time under these conditions. Thus, *p*-chloroaniline (**6g**), which is the most susceptible substrate in the reaction, was treated with 3 equiv of NO for 96 h in the presence of 0.1 equiv of O_2 to give chlorobenzene in 87% yield. Compound **6d** afforded the product in 66% yield under the same conditions (Table 8). Thus, 3 equiv of NO is sufficient for the completion of the reaction, although the reaction rate was too slow to clarify the real stoichiometry.

The above reaction seems to proceed by two steps, that is, the formation of phenyl diazonium salts and succeeding reductive denitrogenation. In addition, the necessity of a trace amount of O_2 for the deamination indicates that catalytic amounts of N_2O_3 (or NO_2) plays a crucial role for the reaction. Furthermore, 3 equiv of NO seems to be necessary, although there remains the possibility that a smaller amount is sufficient for completion of the reaction. Therefore, the total reaction scheme may be summarized as shown in Scheme 3. A detailed reaction

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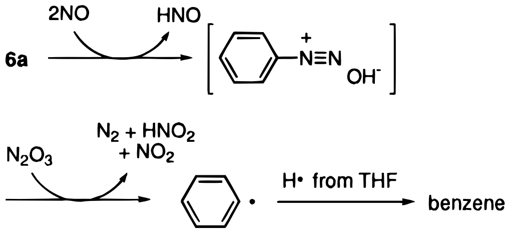
(17) It was reported that phenyldiazonium salts that have an electron-donating group on the *meta* position were unstable compared to their *o*- or *p*-substituted counterparts. See: Swain, C. G.; Sheats, J. E.; Harbison, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 783.

(18) Westheimer, F. H.; Segel, E.; Schramn, R. J. *J. Am. Chem. Soc.* **1947**, *69*, 773.

(19) The low yield of the azo product **8a** suggests the possibility that all of the precipitate may not be the corresponding diazonium salt. Drago *et al.* have shown that primary and secondary amines reacted with NO at −78 °C in ether to form precipitates that were characterized as complexes of amines and NO: (a) Drago, R. S.; Paulik, F. E. *J. Am. Chem. Soc.* **1960**, *82*, 96. (b) Drago, R. S.; Karstetter, B. R. *J. Am. Chem. Soc.* **1961**, *83*, 1819. Our precipitate might comprise this type of complex, although it was reported in ref 19b that aniline did not form the stable one.

Scheme 3



mechanism is now under investigation.

Summary and Conclusions

In this paper, we have described two reactions of amines with NO and the effect of O_2 on these reactions. Hantzsch dihydropyridines aromatize in quantitative yields by the reaction with NO in the absence of O_2. The reaction proceeded smoothly without any side reaction, and the products are isolated as almost pure compounds only after solvent evaporation. Thus, this reaction system might be superior to previous methods for aromatization. Aromatic primary amines react with NO in THF in the presence of catalytic amounts of O_2 to undergo deamination. This reaction is unique in that N_2O_3 (or NO_2) acts as a reductant-like species and that the addition of a sufficient amount of oxygen decreases the reaction yields instead. It was reported that nitrosoalkanes reacted with NO to bring about the formation of alkyl radicals *via* diazonium intermediates.[20] Our reaction might proceed through a similar mechanism, though the details need further investigation. Deamination of aromatic primary amines is an important substitution reaction,[21] and there are many reports concerning the hydrogen donors including hypophosphorous acid as a standard.[22] Our reaction system seems to be of synthetic use since the reaction is performed under mild conditions[23] using a gaseous reagent. The applications of these reactions to other amino compounds are now in progress.

Experimental Section

A melting point was taken on a Büchi 535 micro melting point apparatus and is uncorrected. The mass spectrum was recorded on JEOL JMS-SX102A instrument. The nuclear magnetic resonance spectra (NMR) were measured with JEOL GX400 and LA500 spectrometers using tetramethylsilane as an internal standard. HPLC analysis was performed using JASCO TRI ROTAR-V pump and JASCO UVIDEC-100-V UV spectrophotometer.

Materials. All chemicals are of analytical grade and were used as received. It was necessary, however, to distill the reaction solvents freshly in order to obtain reproducible results. Nitric oxide gas (99.9%) was purchased from Takachiho Chemical Company Ltd. and was passed through a column of 4−8 mesh soda lime to remove NO_x impurities. Hantzsch dihydropyridines were synthesized by the reported methods.[9,24]

General Procedure for the Aromatization of Hantzsch Dihydropyridines. A Hantzsch dihydropyridine **1** (50 μmol) was placed in a two-necked flask (vol. ca. 35 mL) equipped with a septum ruber and three-way stopcock, one way of which was attached to an Ar balloon, and the other jointed to a pump. The flask was degassed under vacuo and filled with Ar gas. These operations were repeated five times. Freshly distilled 1,2-dichloroethane (2.5 mL) was added, the solution was bubbled with dry Ar gas for 20 min, and then the flask was sealed. NO gas was through a column of soda lime, measured at 22.4 mL using a Hamilton gas-tight syringe, and then added to the reaction vessel. The inner pressure is estimated at about 160 kPa. The reaction mixture was allowed to react for several hours at room temperature. Then Ar was bubbled for degassing of excess NO, and the solvent was evaporated to leave almost pure compound **2**, which was further purified with a short column of alumina. Among the aromatized products, **2a**−**d**,**f**,**h** were identified by comparing their physical and spectrometric data with reported data.[10, 24] Compound **2g** was a known compound as an oil, but its spectral data were not reported. **2g**: ^{1}H-NMR ($CDCl_3$) δ 1.53 (6H, d, $J = 7.3$ Hz), 2.80 (6H, s), 3.59 (1H, sep, $J = 7.3$ Hz); ^{13}C-NMR ($CDCl_3$) δ 20.34, 24.56, 33.88, 106.43, 115.29, 164.13; HRMS m/z (M^+) calcd for $C_{12}H_{13}N_3$ 199.1109, found 199.1119. Compound **2e** is a new compound obtained as an oil. **2e**: ^{1}H-NMR ($CDCl_3$) δ 1.37 (6H, t, $J = 7.2$ Hz), 1.78−2.22 (6H, m), 2.48 (6H, s), 2.77 (1H, m), 4.39 (4H, q, $J = 7.2$ Hz), 5.68 (2H, bs); ^{13}C-NMR ($CDCl_3$) δ 14.02, 22.66, 26.26, 26.81, 31.22, 40.00, 61.65, 126.35, 126.54, 127.14, 148.29, 154.80, 169.23; HRMS m/z (M^+) calcd for $C_{19}H_{25}NO_4$ 331.1783, found 331.1754.

General Procedure for the Deamination of Aromatic Amines. The sampling and degassing processes were as same as those of Hantzsch dihydropyridines. Freshly distilled THF (2.5 mL) was added, and the solution was bubbled with dry Ar gas for 20 min. Then the flask was sealed, and O_2 (1 μL) was added with a micro syringe. NO gas was added to the reaction vessel, and the reaction mixture was allowed to stand for several hours at room temperature. During this time, formation of a precipitate was observed in the solvent, which was dissolved through the reaction progress. Then Ar was bubbled for degassing of excess NO. Thereafter, the solvent was evaporated off, and the product yield was determined by NMR using mesitylene as an internal standard or was estimated by HPLC using naphthalene as an internal standard.

Diazo Coupling of an Intermediate of 6a. Aniline (0.2 mmol) was allowed to react in THF (10 mL) with NO (90 mL) and O_2 (1 μL) under the same conditions mentioned above for 10 min. A precipitate thus formed was filtered and dissolved in 5 mL of 25% aqueous NaOAc solution. Then dimethylaniline (0.2 mmol) was added, and the mixture was allowed to react for 10 min at room temperature. The solution was made basic with 1 N aqueous NaOH, and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and evaporated off to leave a residue, which was chromatographed on silica gel to give 2.5 mg (6%) of orange needles **8a**: mp 113−115 °C (lit.[18] mp 114−117 °C); ^{1}H-NMR ($CDCl_3$) δ 3.08 (6H, s), 6.76 (2H, d, $J = 8.0$ Hz), 7.38 (1H, m), 7.47 (2H, m), 7.83 (2H, m), 7.88 (2H, d, $J = 8.0$ Hz).

The Reaction of 6d in the Presence of Diphenyl Disulfide. The reaction was carried out under the same conditions as mentioned in the above general procedure except that 2 equiv of diphenyl disulfide was added in the reaction mixture and benzene was used as solvent. The structures of 4-(methylthio)biphenyl and 1-(methylthio)-4-(phenylthio)benzene were determined by comparing physical and spectrometric data with the reported data.[25,26]

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(23) It was revealed that the same reaction process was applied to 2-aminothiazole and 3-amino-1,2,4-triazines, which gave poor results by the use of the conventional methods, to give the corresponding deamination products in good yields. The detailed results will be reported in a near future.

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