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Amidines. II. Preparation of Unsymmetrical N^1,N^2-Disubstituted Amidines

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Unsymmetrical N^1,N^2-disubstituted amidines were prepared by conventional and newly developed methods. Reaction of N^1-tosyl-N^1,N^2-diarylacetamidines and arylamines gave unsymmetrical acetamidines in the presence of basic catalysts, and N^1-acyl-N^1,N^2-di(*p*-nitrophenyl)formamidines and arylamines gave unsymmetrical formamidines under neutral conditions.

Unsymmetrical amidines exist as tautomeric mixtures in solution owing to proton transfer between the two nitrogen atoms, and it was proved on the basis of proton nuclear magnetic resonance (^{1}H-NMR) evidence that the tautomer in which the hydrogen is attached to the more basic nitrogen atom is predominant.

Keywords N^1-aryl-N^2-(*p*-nitrophenyl)acetamidine; N^1-aryl-N^2-(*p*-nitrophenyl)formamidine; N^1-alkyl-N^2-(*p*-nitrophenyl)-formamidine; aminolysis; *N*-tosylacetamidine; *N*-acylformamidine; tautomerization; ^{1}H-NMR

Hydrolysis of N^1,N^2-disubstituted amidines affords amines and *N*-acylamines. In the case of unsymmetrical amidines, there are two possible pathways. One of them gives the more basic amine and the acyl derivative of the less basic amine, and the other gives the less basic amine and the acyl derivative of the more basic amine. In the present work, preparation of unsymmetrical N^1,N^2-disubstituted amidines, especially those having a *p*-nitrophenyl or 2,4-dinitrophenyl group as a substituent, was undertaken for kinetic examination of the acid hydrolysis of unsymmetrical amidines.

In general, four methods are known for the preparation of unsymmetrical N^1,N^2-disubstituted amidines. Method A: reaction of imidoyl chloride and an amine. Method B: reaction of alkyl imidate and an amine. Method C: exchange of the amino moiety of an amidine. Method D: Beckmann rearrangement of a ketoxime benzenesulfonate in the presence of an amine. In this work, we established a new method for the preparation of unsymmetrical amidines, *i.e.*, reaction of N^1-(*o*-nitrobenzoyl)-N^1,N^2-di (*p*-nitrophenyl)formamidine (**6**) and arylamines under neutral conditions, and reaction of N^1-tosyl-N^1,N^2-diarylacetamidines (**7**) and arylamines under basic conditions, to give unsymmetrical N^1,N^2-disubstituted formamidines and acetamidines, respectively.

Preparation of Unsymmetrical N^1,N^2-Disubstituted Amidines Reaction of amines and imidoyl chloride derived from *N*-acetyl or *N*-benzoylamine (method A) provides one of the routes for the preparation of unsymmetrical amidines.[1] N^1-Aryl-N^2-(*p*-nitrophenyl)acetamidines (**8**) could not be prepared, however, from *N*-acetyl-*p*-nitroaniline and arylamines by this route.

Roberts *et al.*[2] reported the preparation of unsymmetrical diarylformamidines by the reaction of ethyl *N*-arylformimidate and arylamines in the absence of an acidic catalyst (method B). They claimed that no exchange of the arylamino moiety occurred when a diarylformamidine was treated with an arylamine in the absence of acid. They obtained N^2-(*p*-nitrophenyl)-N^1-phenylformamidine (**4c**) by the reaction of ethyl *N*-phenylformimidate and *p*-nitroaniline, though, only after repeated recrystallization of the crude product, and they noted the formation of N^1,N^2-di(*p*-nitrophenyl)formamidine (**4e**) as a by-product in the reaction. As already pointed out by Taylor and Ehrhart,[3] the reaction of alkyl *N*-arylacetimidates and arylamines hardly takes place in the absence of a catalytic acid.

A mixture of three amidines [N^1,N^2-di(*p*-chlorophenyl)-acetamidine (**3**), N^1-(*p*-methoxyphenyl)-N^2-(*p*-chlorophenyl)acetamidine (**1**) and N^1,N^2-di(*p*-methoxyphenyl)acetamidine (**2**) in a ratio of 19 : 49 : 32] was obtained when a ben-

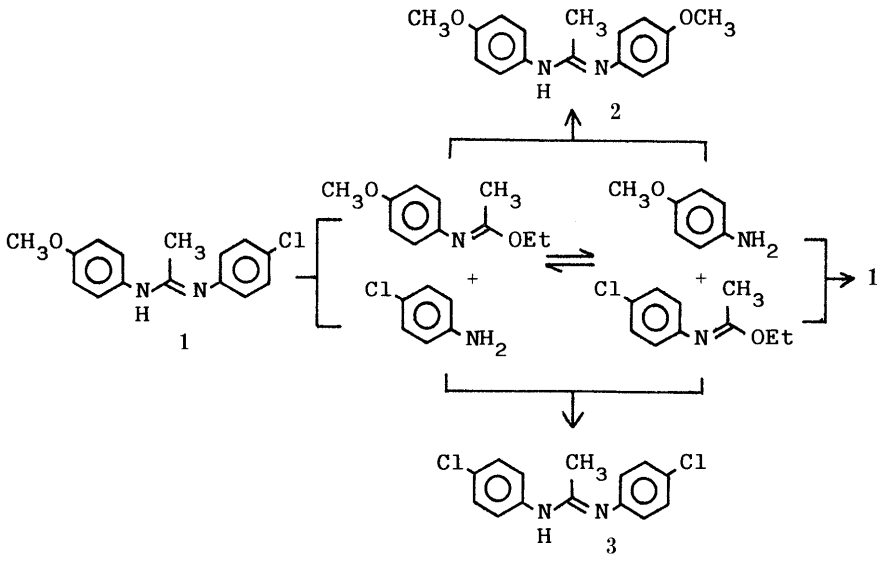


Chart 1

zene solution of ethyl *N*-(*p*-methoxyphenyl)acetimidate and *p*-chloroaniline was refluxed in the presence of *p*-toluenesulfonic acid (Chart 1). Compound **1** was isolated from the mixture by column chromatography. A mixture of the same three amidines (15:55:30) was obtained from ethyl *N*-(*p*-chlorophenyl)acetimidate and *p*-anisidine by the same treatment. When a benzene solution of **3** and *p*-anisidine was refluxed in the presence of *p*-toluenesulfonic acid, a mixture of the same three amidines (42:36:12) was obtained. A mixture of **1** and **2** (12:88) was obtained from **2** and *p*-chloroaniline by the same treatment. The results imply that the exchange of the arylamino moiety in an imidate is faster than that in an amidine, and that the exchange of the arylamino moiety in an imidate is faster than the formation of an amidine in the reaction of imidate and arylamines in the presence of a catalytic acid. Hand and Jencks[4] reported the existence of a pre-equilibrium involving an exchange of the imidate amino moiety before appreciable formation of the amidine in the reaction of ethyl benzimidate and amine under acidic conditions (Chart 1).

Hinkel *et al.*[5] obtained N^1-benzhydryl-N^2-phenylformamidine on heating of a mixture of N^1-benzhydrylformamidine and aniline (method C). Oszczapowicz and Orlinski[6] reported a preparative route to unsymmetrical formamidines by the reaction of N^1,N^2-diphenylformamidine and secondary aliphatic amines. Oszczapowicz[7] obtained unsymmetrical acetamidines in a similar manner. This method would be suitable for the preparation of unsymmetrical formamidines from symmetrical diarylformamidines having electron-withdrawing aryl substituents and reactive aliphatic amines. Thus, N^1-(*p*-methylbenzyl)-N^2-(*p*-nitrophenyl)formamidine (**5a**) was obtained by the reaction of N^1,N^2-di(*p*-nitrophenyl)formamidine (**4e**) with *p*-methylbenzylamine in dimethylformamide (DMF) solution. Other unsymmetrical N^1,N^2-disubstituted formamidines, N^1-alkyl-N^2-(*p*-nitrophenyl)formamidines (**5**), were prepared in a similar manner (Chart 2). The reaction of **4e** and arylamines proceeded with great difficulty. Prolonged heating of the reaction mixture caused the formation of symmetrical diarylformamidines derived from further exchange of the *p*-nitrophenyl group of the unsymmetrical amidine by the arylamine. N^1-Aryl-N^2-(*p*-nitrophenyl)formamidines (**4**) were obtained in very low yields by the reaction of **4e** and arylamine (*e.g.*, *p*-anisidine and *p*-toluidine) at room temperature. This method would

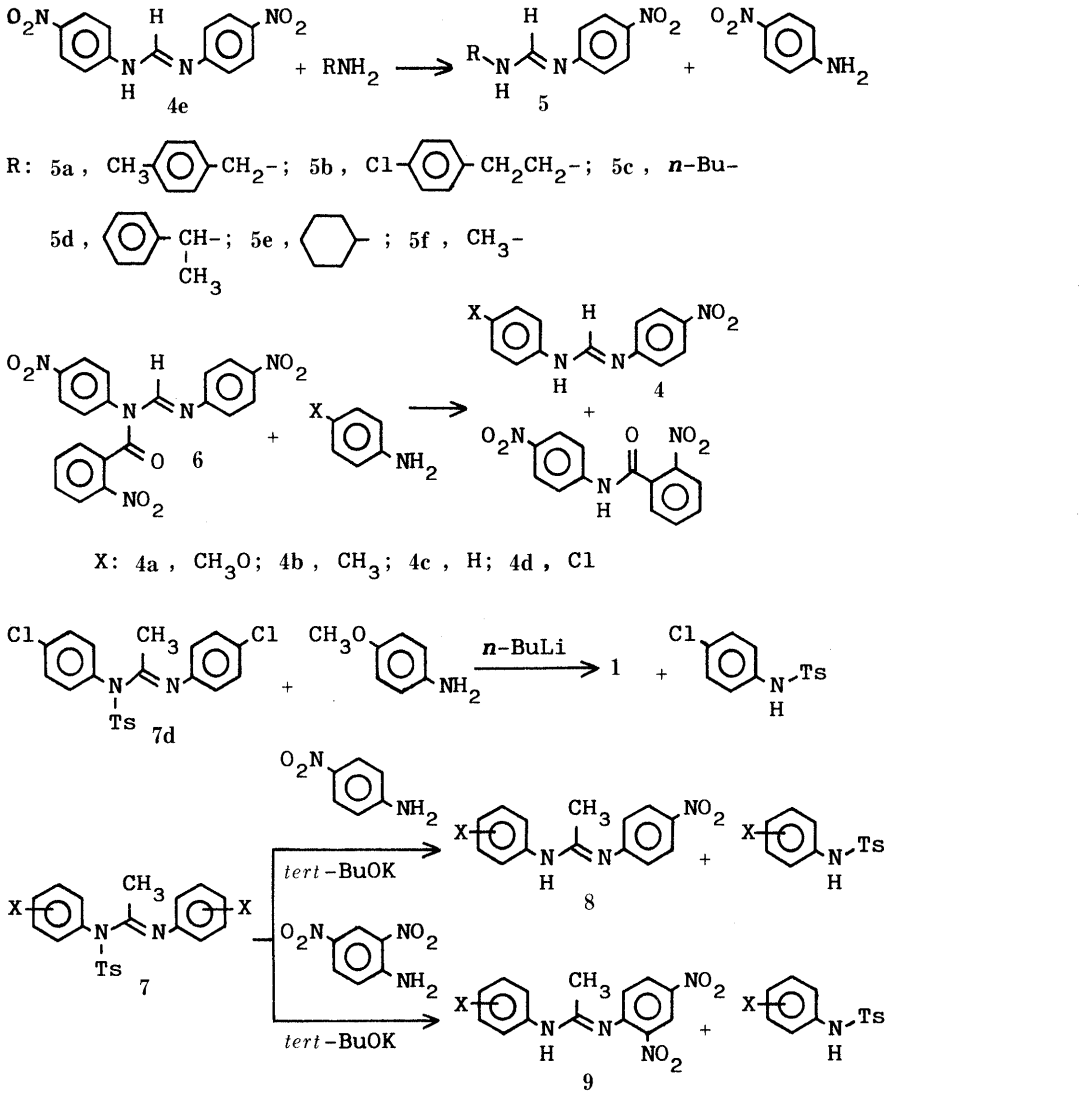


Chart 2

be unsuitable for preparation of unsymmetrical acetamidines because of the less electrophilic character of the amidine central carbon of acetamidines than that of formamidines.

The electrophilic character of the central carbon of N^1-acyl derivatives of amidines is expected to be much greater than that of the amidines themselves. Thus, the acid hydrolysis of N^1-acyl-N^1,N^2-diarylamidines proceeded much faster than that of the corresponding N^1,N^2-diarylamidines, and attack of a water molecule was proved to take place exclusively at the central carbon.[8] Although alkaline hydrolysis of N^1-acyl-N^1,N^2-diarylformamidines took place mainly at the amide carbonyl group to give N^1,N^2-diarylamidines and a carboxylic acid, hydroxide ion attacked the central carbon of N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine to a small extent.[8]

The reaction of arylamines and N^1-(*o*-nitrobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine (**6**) proceeded much faster than that of arylamines and **4e**, and the attack of the arylamines took place mainly at the central carbon to give N^1-aryl-N^2-(*p*-nitrophenyl)formamidines (**4**) (Chart 2).

The electrophilic character of the central carbon of N^1-acyl-N^1,N^2-diarylacetamidines would be less than that of the corresponding N^1-acylformamidines. Thus, acid hydrolysis of N^1-acyl-N^1,N^2-diarylacetamidines proceeded at slower rates than those of the corresponding N^1-acylformamidines.[8] Alcoholysis of N^1-tosyl-N^1,N^2-diarylacetamidines in ethanol solution in the presence of sodium ethoxide gave ethyl *N*-arylacetimidates and *N*-tosylarylamines in quantitative yield. Ethoxide ion attacked exclusively the central carbon.[8]

Compound **1** was obtained in good yield on allowing a tetrahydrofuran (THF) solution of N^1-tosyl-N^1,N^2-di(*p*-chlorophenyl)acetamidine (**7d**) and *p*-anisidine to stand in the presence of *n*-butyllithium at room temperature. The formation of **2** as a by-product was not detected. Use of *n*-butyllithium in the reaction of N^1-tosyl-N^1,N^2-diarylacetamidine (**7**) and *p*-nitroaniline as a basic catalyst caused a polymerization of the substrate. A small amount of *p*-nitrosoaniline was isolated from the mixture in which *p*-nitroaniline was kept in THF solution in the presence of *n*-butyllithium. N^1-Aryl-N^2-(*p*-nitrophenyl)acetamidines (**8**) were prepared by the reaction of **7** and *p*-nitroaniline in the presence of potassium *tert*-butoxide. N^1-Aryl-N^2-(2,4-dinitrophenyl)acetamidines (**9**) were prepared in a similar manner (Chart 2).

N^1-(*m*-Chlorophenyl)-N^2-(*p*-nitrophenyl)acetamidine (**8e**) and N^1-(*p*-cyanophenyl)-N^2-(*p*-nitrophenyl)acetamidine (**8g**) could not be prepared by this method because the corresponding symmetric amidines could not be obtained by the reaction of ethyl orthoacetate and *m*-chloroaniline or *p*-aminobenzonitrile. An examination of the reaction between N^1-tosyl-N^1,N^2-di(*p*-nitrophenyl)acetamidine (**7g**) and arylamines was undertaken to seek another possible route for the preparation of **8**. Compound **7g** was prepared by the Beckmann rearrangement of *p*-nitroacetophenoxime tosylate in the presence of the sodium salt of *N*-tosyl-*p*-nitroaniline.[9] Compound **7g** is, however, unsuitable as a starting material for preparative work because it is almost insoluble in all solvents examined. Compounds **8e** and **8g** were prepared in low yields by the reaction of ethyl *N*-(*p*-nitrophenyl)acetimidate and corresponding arylamines (Chart 3).

Compounds **4** could not be obtained by the reaction of N^1-tosyl-N^1,N^2-diarylformamidines and *p*-nitroaniline even in the presence of a basic catalyst. When a THF solution of N^1-tosyl-N^1,N^2-di(*p*-tolyl)formamidine and *p*-nitroaniline was kept for 1 d in the presence of potassium *tert*-butoxide at room temperature, remaining *p*-nitroaniline and a small amount of *N*-tosyl-*p*-toluidine were isolated, but **4b**, which was expected to be formed, could not be detected in the reaction mixture. The reason for these results is not clear.

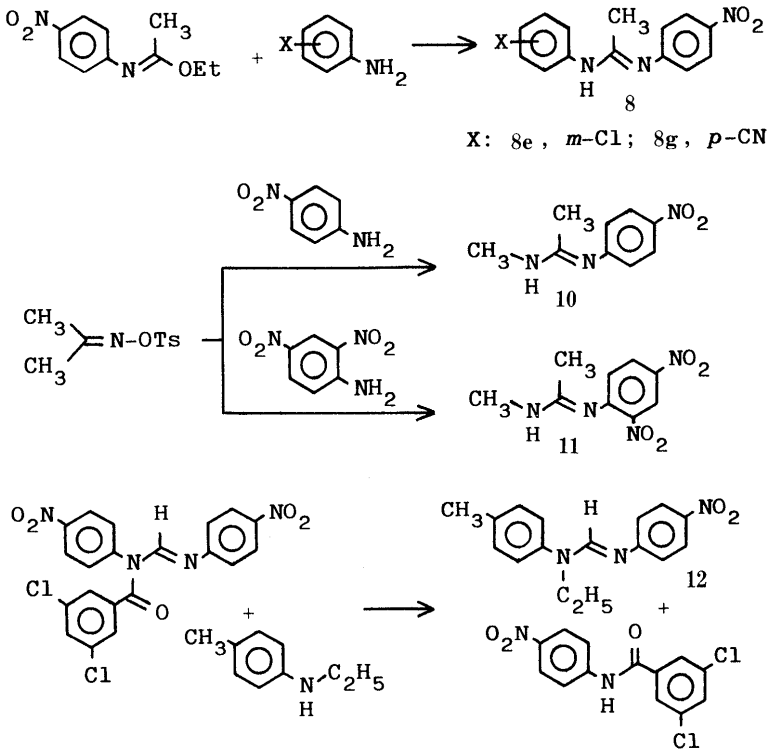


Chart 3

Oxley and Short[9] prepared unsymmetrical amidines by Beckmann rearrangement of ketoxime benzenesulfonate in the presence of amines (method D). N^1-Methyl-N^2-(*p*-nitrophenyl)acetamidine (**10**) and N^1-methyl-N^2-(2,4-dinitrophenyl)acetamidine (**11**) were prepared by the reaction of acetoxime tosylate and the corresponding arylamines (Chart. 3).

Tautomerization of Unsymmetrical Amidines The nuclear magnetic resonance (NMR) spectra of N^1,N^2-disubstituted amidines showed temperature-dependent patterns, probably arising from three separate phenomena. First, change between (*E*)- and (*Z*)-configuration of the imino double bond. Second, conformational change arising from free rotation around the single bond between amino nitrogen and the amidine central carbon. Third, proton transfer between the two nitrogen atoms.

Hegarty and Chandler[10] prepared trisubstituted amidines having (*Z*)-configuration by the reaction of aryl isocyanides and secondary amines at low temperature. They pointed out that the (*Z*)-isomer is easily converted irreversibly into the corresponding (*E*)-isomer. Examples of temperature dependence of NMR spectra of amidines arising from free rotation around the N^1–C single bond have been reported by many investigators, *e.g.*, Bertelli and Gerig,[11] Harris and Wellman,[12] Rappoport and Ta-Shma,[13] and Oszczapowicz *et al.*[14] Differencies in chemical shifts of ^{13}C signals of the N^2-aryl group of conformational isomers of N^1-alkyl-N^1,N^2-diarylamidines were observed to be about 0.7 ppm,[14] and all trisubstituted amidines examined were proved to exist as the (*E*)-isomer in solution.[14] The temperature dependence of ^{1}H-NMR spectra of N^2-*tert*-butyl-N^1,N^1-dimethylamidine[12] and trisubstituted N^2-arylamidines[13] was proved to be due to free rotation around the N^1–C bond and not to (*E*)- and (*Z*)-isomerization.

The (*E*)- and (*Z*)-isomerization of N^1,N^2-disubstituted amidines would occur more easily than that of trisubstituted amidines owing to the combination of free rotation around the N^1–C bond and proton transfer between the two nitrogen atoms. Jackman and Jen[15] pointed out that 2-phenyliminopyrrolidine contained a small portion of (*Z*)-isomer in solution, judging from NMR evidence. They reported that the ^{13}C chemical shifts of corresponding atoms in the two isomers lie within 1 ppm.

In N^1,N^2-disubstituted amidines having an electron-withdrawing group on one substituent, *e.g.*, N^1-(*p*-methylphenyl)-N^2-(*p*-nitrophenyl)formamidine (**4b**), the tautomer having a *p*-nitrophenylimino structure would predominate over the other isomer, N^1-(*p*-nitrophenyl)-N^2-(*p*-methylphenyl)formamidine (**4b′**), owing to resonance stabilization, and the NMR signal of 2″-H can be expected to be observed at higher applied magnetic field than that of 2′-H of the isomer (Chart 4). Oszczapowicz *et al.*[16] reported that the signals of *o*-positions of the N^2-aryl group of N^1-alkyl-N^1,N^2-diarylamidines are observed at higher applied magnetic field than those of the *o*-positions of the N^1-aryl group.

For comparison of the effects of rotational and proton transfer tautomerizations upon the NMR, N^1-ethyl-N^1-(*p*-methylphenyl)-N^2-(*p*-nitrophenyl)formamidine (**12**) was prepared by the reaction of N^1-(3,5-dichlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine (Chart 3). The ^{1}H-NMR spectrum (acetone-d_6, 400 MHz) of **12** showed a 3″-H and 5″-H signal at δ 8.15, a rather broad 2″-H and 6″-H signal at δ 7.23, and signals of 2′-H and 6′-H, and 3′-H and 5′-H at δ 7.26 and 7.29 at 24 °C. The signals were slightly shifted to lower applied magnetic field on the whole at lower temperature. At −50 °C, separate signals of 3″-H and 5″-H were observed at δ 8.26 and 8.32 (relative intensity, 17 : 3) and broad signals of the other aromatic protons were observed at δ 7.3—7.5. The spectrum (400 MHz) of **4b** in acetone-d_6 solution showed coalesced signals of 3″- and 5″-H of **4b** and 3′- and 5′-H of **4b′** at δ 8.18 and broad signals of the other aromatic protons were observed at δ 7.08—7.18 and 7.4—7.6 at 24 °C. At −35 °C, a rather broad coalesced signal of 3″- and 5″-H of **4b** and 3′- and 5′-H of **4b′** was observed at δ 8.23 and a small signal of 2′- and 6′-H of **4b′** was observed at δ 7.87, while broad signals of the other aromatic protons were observed at δ 7.1—7.3 and 7.3—7.6. In the ^{1}H-NMR spectrum of **12** which showed a temperature-dependent pattern due to free rotation around the N^1–C bond, signals could not be detected in the region in which the signal of 2′- and 6′-H of **4b′** was observed (near δ 7.7—7.9). The temperature-dependent pattern of ^{1}H-NMR spectra of unsymmetrical N^1,N^2-disubstituted amidines was concluded to be attributable mainly to proton transfer between the two nitrogen atoms.

Typical ^{1}H-NMR data for unsymmetrical amidines are shown in Table I. At −50 °C, the ^{1}H-NMR (methanol-d_4, 400 MHz) of **8a** showed the pattern of a mixture of N^1-(*p*-methoxyphenyl)-N^2-(*p*-nitrophenyl)acetamidine (**8a**) and N^1-(*p*-nitrophenyl)-N^2-(*p*-methoxyphenyl)acetamidine (**8a′**) suggesting that the proton transfer between the two nitrogen atoms is slow enough to detect under these conditions. Relative integrated intensities of the signals showed that the mixture consisted of **8a** and **8a′** in a ratio of 3 : 2. At −20 °C, the signals of the 2′-, 6′- and 2″-, 6″-H of **8a** became somewhat broader owing to the intermediate rate (on the NMR time scale) of proton transfer. At 25 °C, ^{1}H-NMR of **8a** (methanol-d_4, 400 MHz) showed only two definite signals at δ 6.86 (3′- and 5′-H) and 8.15 (3″- and 5″-H) in the aromatic proton region. ^{1}H-NMR (chlo-

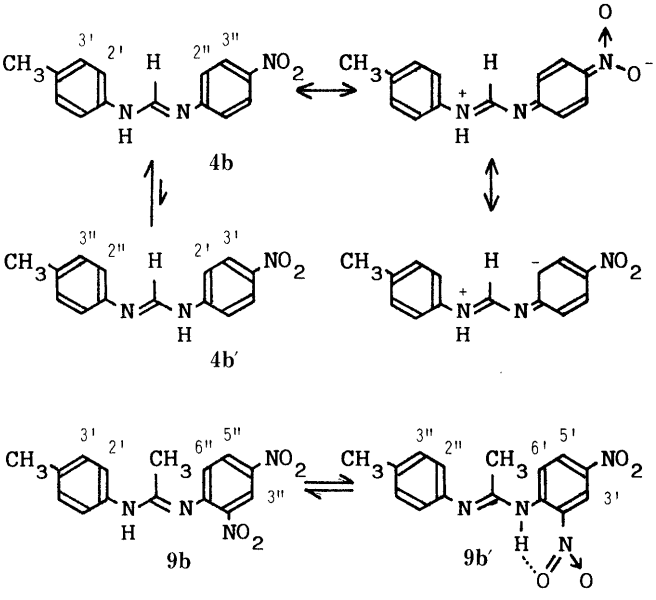
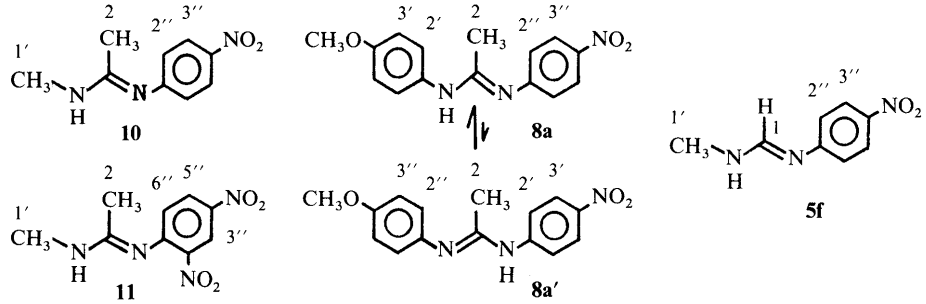


Chart 4

TABLE I. Chemical Shifts (δ) of ^{1}H-NMR Signals of Unsymmetrical N^1,N^2-Disubstituted Amidines in CD_3OD



	MHz	Temp. (°C)	1	2	1′	2′	3′	2″	3″	5″	6″	OCH_3 or aryl CH_3
10	60	37		1.83	2.85			6.93	8.15			
11	60	37		1.87	2.80				8.65	8.25	7.07	
5f	60	37	7.88		2.95			7.08	8.12			
8a	400	−50		1.98		7.52	6.85	6.95	8.17			3.74
8a′	400	−50		1.96		7.94	8.18	6.75	6.86			3.75
9b	400	25		2.04		7.44	7.08		8.74	8.33	7.12	2.28

roform-*d*, 60 MHz) of **8a** showed a coalesced pattern of a mixture of **8a** and **8a′** (in which **8a** is predominant) at 37 °C: δ 3.80 (OCH_3), 6.87 (3′- and 5′-H), 7.10 (2″- and 6″-H), 7.23 (2′- and 6′-H) and 8.15 (3″- and 5″-H). This suggests that the proton transfer takes place rather rapidly on the NMR time scale under the conditions used. The ^{1}H-NMR spectra (chloroform-*d*, 60 MHz) of **8b**, **8c** and **8d** showed similar patterns to those of **8a** in the aromatic proton region (results not shown), and the less electron-releasing the substituent on the N^1-aryl group, the broader the signals of 2″- and 6″-H of **8**, suggesting that electron-releasing substituents on the N^1-aryl group increase the rate of proton transfer between the two nitrogen atoms.

Thus, unsymmetrical amidines were proved to exist as a tautomeric mixture, and the isomer in which the transferable hydrogen atom is attached to the more basic nitrogen atom is predominant. Jackman and Jen[15] pointed out that the predominant tautomer of 2-phenyliminopyrrolidine is the imino form rather than amino form (2-phenylamino-1-pyrroline) on the basis of NMR evidence. Gautier *et al.*[17] claimed that *N*-phenylbenzamidine should be expressed as 1, *N*′-diphenylmethanimidamide, H_2N–C(Ph)=N–Ph, on the basis of infrared (IR) evidence, and Cook *et al.*[18] pointed out that *N*-phenylacetamidine should be expressed as *N*′-phenylethanimidamide, H_2N–C(Me)=N–Ph, on the basis of ultraviolet (UV) spectral evidence.

The ^{1}H-NMR spectrum (methanol-d_4, 400 MHz) of **9b** showed that no **9b′** exists in this solution (Table I). In chloroform-*d* solution, however, the compound exists as a mixture of **9b** and **9b′** in a ratio of about 1 : 1 at −20 °C (see Experimental). Probably **9b′** is stabilized by chelation in chloroform-*d* solution (Chart 4).

Experimental

All melting points are uncorrected. ^{1}H-NMR spectra were recorded on JEOL PMX-60 and JEOL GX-400 NMR spectrometers with tetramethylsilane as an internal standard. The following abbreviations are used: s (singlet), d (doublet), dd (double doublet), t (triplet), br (broad) and m (multiplet). Compounds **7a**—**d** were prepared according to a previous paper.[19] The *N*-acylarylamines, *N*-tosylarylamines and amidines formed were identical with corresponding authentic samples on the basis of comparison of their IR spectra or mixed melting point measurement.

Preparation of 1 by the Reaction of Ethyl *N*-(*p*-Methoxyphenyl)-acetimidate and *p*-Chloroaniline *p*-Toluenesulfonic acid monohydrate (0.48 g, 2.5 mmol) was dried by repeated addition of dry benzene and subsequent evaporation, and was added to a solution of ethyl *N*-(*p*-methoxyphenyl)acetimidate (4.83 g, 25 mmol) and *p*-chloroaniline (3.19 g, 25 mmol) in 2.5 ml of benzene. The mixture was refluxed for 3 h, and then 40 ml of benzene was added. The solution was extracted successively with 30 and 10 ml of 2 N HCl. The combined HCl layer was made alkaline with $NaHCO_3$, and the mixture was extracted with ether. The ether layer was concentrated under reduced pressure, and the residue was steam-distilled to remove remaining *p*-chloroaniline. The remaining fraction was extracted with ether. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was subjected to column chromatography (Al_2O_3) successively with petroleum benzin–benzene (1 : 2) and benzene–AcOEt (9 : 1). From the first fraction, 0.61 g of **3** was obtained. From the second fraction, 1.20 g (18%) of **1** was obtained after recrystallization from petroleum benzin. mp 112 °C. *Anal.* Calcd for $C_{15}H_{15}ClN_2O$: C, 65.57; H, 5.50; N, 10.20. Found: C, 65.61; H, 5.49; N, 10.21. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 1.95 (3H, s, 2-position), 3.77 (3H, s, OCH_3), 6.80, 6.97, 7.10, 7.20 (each 2H, d, J=8 Hz, aryl H).

The sample used for products analysis by ^{1}H-NMR was prepared as follows: dried TsOH (prepared from 0.095 g of TsOH·H_2O) was added to a solution of ethyl *N*-(*p*-methoxyphenyl)acetimidate (0.965 g, 5 mmol) and *p*-chloroaniline (0.638 g, 5 mmol) in 2 ml of benzene. The mixture was refluxed for 3 h and then 20 ml of benzene was added. The whole was extracted successively with 30, 10, and 10 ml of 2 N HCl (remaining imidate was converted to arylamine and AcOEt by this operation). The HCl layer was made alkaline with $NaHCO_3$, and the mixture was extracted with ether. The ether layer was concentrated under reduced pressure, and the residue was steam-distilled. The remaining fraction was extracted with ether, and the ether layer was dried over K_2CO_3. A part of the solution was concentrated under reduced pressure, and the residue was subjected to ^{1}H-NMR analysis (dimethyl sulfoxide-d_6 (DMSO-d_6)–D_2O, at 60 °C). The samples for ^{1}H-NMR analysis of the reaction of ethyl *N*-(*p*-chlorophenyl)acetimidate (0.988 g, 5 mmol) and *p*-anisidine (0.615 g, 5 mmol); **2** (1.350 g, 5 mmol) and *p*-chloroaniline (0.640 g, 5 mmol); **3** (1.395 g, 5 mmol) and *p*-anisidine (0.615 g, 5 mmol) were prepared in the same manner. The ^{1}H-NMR (DMSO-d_6–D_2O, 400 MHz at 60 °C) signal of 2-H (**3**, δ 1.91; **1**, 1.89 and **2**, 1.86) was used as the integration standard. The results are described in the main text.

Preparation of 5 An appropriate amine (0.05 mol) was added to a hot solution of **4e** (14.30 g, 0.05 mol) in 50 ml of DMF. The red mixture was allowed to stand overnight at room temperature, and then concentrated under reduced pressure. Water (50 ml) was added to the residue, and the supernatant liquid was discarded by decantation to remove any remaining DMF. Ether (100 ml) was added to the residue, and the mixture was filtered. Then 100 ml of 1 N HCl was added with stirring to the ether layer of the filtrate under ice cooling. In the cases of **5a**, and **5b**, the hydrochloride precipitated as a white powder, and was collected. Usual

treatment of the precipitate gave **5a** (9.02 g, 67%) and **5b** (8.05 g, 53%), respectively. In the cases of **5c**—**e**, the hydrochloride separated as an oil. The supernatant was removed by decantation, and the residue was treated as usual to give **5c** (8.63 g, 78%), **5d**, (3.90 g, 29%) and **5e**, (6.68 g, 54%), respectively. The properties of **5a**—**e** were as follows: **5a**, mp 125 °C (AcOEt). *Anal.* Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 67.09; H, 5.60; N, 15.54. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.33 (3H, s, CH_3), 4.53 (2H, s, CH_2), 6.97 (2H, d, J=9 Hz, 2″- and 6″-positions), 7.17 (4H, s, aryl H of N^1-substituent), 7.75 (1H, s, 1-position), 8.10 (2H, d, J=9 Hz, 3″- and 5″-positions). **5b**, mp 120.5 °C (AcOEt). *Anal.* Calcd for $C_{15}H_{14}ClN_3O_2$: C, 59.31; H, 4.65; N, 13.83. Found: C, 59.38; H, 4.62; N, 13.76. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.93 (2H, t, J=7 Hz, $ClC_6H_4C\underline{H}_2CH_2$–), 3.70 (2H, br t, J=7 Hz, $ClC_6H_4CH_2C\underline{H}_2$–), 6.97 (2H, d, J=9 Hz, 2″- and 6″-positions), 7.20 and 7.30 (each 2H, d, J=9 Hz, aryl H of N^1-substituent), 7.63 (1H, s, 1-position), 8.13 (2H, d, J=9 Hz, 3″- and 5″-positions). **5c**, mp 89 °C (petroleum benzin). *Anal.* Calcd for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.75; H, 6.81; N, 18.83. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 0.73—1.83 (7H, m, $C\underline{H}_3C\underline{H}_2C\underline{H}_2$–$CH_2$–), 3.42 (2H, br t, J=6 Hz, –$C\underline{H}_2$–N), 5.30 (1H, br s. NH), 6.97 (2H, d, J=9 Hz, 2″- and 6″-positions), 7.67 (1H, s, 1-position), 8.08 (2H, d, J=9 Hz, 3″- and 5″-positions). **5d**, mp 102 °C (petroleum benzin). *Anal.* Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 67.00; H, 5.62; N, 15.56. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 1.60 (3H, d, J=7 Hz, CH_3), 5.10 (1H, m, CH), 6.97 (2H, d, J=9 Hz, 2″- and 6″-positions), 7.33 (5H, s, aryl H of N^1-substituent), 7.68 (1H, s, 1-position), 8.10 (2H, d, J=9 Hz, 3″- and 5″-positions). Beside these signals, small signals owing to a conformational isomer were observed at δ: 6.60 (d, J=9 Hz) and 8.07 (d, J=9 Hz). **5e**, mp 115 °C (AcOEt). *Anal.* Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.93; N, 16.99. Found: C, 63.21; H, 6.99; N, 16.89. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 0.75—2.33 (10H, m, 2′,3′,4′,5′,6′-positions), 3.83 (1H, m, 1′-position), 5.07 (1H, br s, NH), 6.97 (2H, d, J=9 Hz, 2″- and 6″-positions), 7.67 (1H, s, 1-position), 8.10 (2H, d, J=9 Hz, 3″- and 5″-positions).

Compound **4e** (28.62 g, 0.1 mol) and dried methylamine hydrochloride (10.13 g, 0.1 mol) were added to 100 ml of pyridine at 80 °C. The yellow mixture became clear after standing for 2 h at 80 °C. The mixture was concentrated under reduced pressure. Xylene (50 ml) was added to the residue, and evaporated off under reduced pressure to remove remaining pyridine. This procedure was repeated three times. Ether and 7% $NaHCO_3$ were added to the residue, and the ether layer was extracted with 150 ml of 1 N HCl. The HCl layer was made alkaline with Na_2CO_3, and extracted with ether. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from a mixture of benzene and petroleum benzin to give 9.90 g (55%) of **5f**. mp 126 °C. *Anal.* Calcd for $C_8H_9N_3O_2$: C, 53.63; H, 5.06; N, 23.45. Found: C, 53.77; H, 5.02; N, 23.33. ^{1}H-NMR is shown in Table I.

Preparation of 6 Thionyl chloride (45 g, 0.33 mol) was added to *o*-nitrobenzoic acid (10.03 g, 0.06 mol) at room temperature. The mixture was heated at 80—85 °C on an oil bath with stirring for 40 min, and concentrated under reduced pressure. Dry benzene (10 ml) was added to the residue, and the mixture was concentrated under reduced pressure to remove remaining $SOCl_2$. This procedure was repeated twice. The residue was dissolved in 30 ml of anhydrous benzene, and the solution was added to a mixture of finely powdered **4e** (14.31 g, 0.05 mol), Et_3N (7.59 g, 0.075 mol) and 70 ml of anhydrous benzene. The mixture was refluxed with vigorous stirring for 3 h. After cooling, the precipitate was collected and washed successively with a small amount of benzene, two portions of 50 ml of H_2O, two portions of 50 ml of 7% $NaHCO_3$, 50 ml of H_2O and a small amount of benzene. Crude **6** (21.08 g) thus obtained was recrystallized from benzene to give 19.77 g (91%) of pure **6** after drying over P_2O_5 under reduced pressure. mp 196.5 °C. *Anal.* Calcd for $C_{20}H_{13}N_5O_7$: C, 55.18; H, 3.01; N, 16.09. Found: C, 55.36; H, 2.97; N, 16.01. ^{1}H-NMR (DMSO-d_6, 60 MHz) δ: 7.15 (2H, d, J=9 Hz, 2″-position), 7.6—8.5 (10H, m, aryl H), 8.80 (1H, s, 1-position).

Preparation of 4a—d A mixture of an arylamine (5 mmol), **6** (2.18 g, 5 mmol) and 15 ml of dioxane was refluxed for 3 h, and concentrated under reduced pressure. Ether (200 ml) was added to the residue, and the precipitate, 2,4′-dinitrobenzanilide, was filtered off with suction, and washed with 100 ml of ether. Then 10 ml of 1 N HCl was added to the combined filtrate under ice cooling with stirring. Deposited precipitate, the hydrochloride of **4a**—**d**, was collected and treated as usual to give **4a**—**d**. The results were as follows: **4a**, yield 0.68 g (50%). mp 153 °C. *Anal.* Calcd for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49. Found: C, 61.76; H, 4.72; N, 15.47. ^{1}H-NMR (CD_3COCD_3–D_2O, 400 MHz) δ: 3.86 (3H, s, OCH_3), 6.93 (2H, d, J=9 Hz, 3′- and 5′-positions), 7.18 (2H, br s, aryl H), 7.60 and 7.85 (2H, each br s, aryl H), 8.20 (2H, d, J=9 Hz, 3″- and 5″-positions), 8.42 (1H, br s, 1-position). **4b**, yield 0.61 g (48%). mp 164 °C. *Anal.* Calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.72; H, 5.03; N, 16.46. ^{1}H-NMR (CD_3COCD_3–D_2O, 400 MHz) δ: 2.30 (3H, s, CH_3), 7.13 (2H, br s, aryl H), 7.16 (2H, d, J=9 Hz, 3′- and 5′-positions), 7.57 (2H, br s, aryl H), 8.19 (2H, d, J=9 Hz, 3″- and 5″-positions), 8.44 (1H, br s, 1-position). **4c**, yield 0.52 g (43%). mp 182 °C (lit. 2, mp 183—5 °C). *Anal.* Calcd for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.76; H, 4.53; N, 17.36. ^{1}H-NMR (CD_3COCD_3–D_2O, 400 MHz) δ: 7.11 (1H, t, J=8 Hz, 4′-position), 7.25 (2H, br s, aryl H), 7.36 (2H, dd, J=7, 8 Hz, 3′- and 5′-positions), 7.58 (2H, br s, aryl H), 8.20 (2H, d, J=9 Hz, 3″- and 5″-positions), 8.45 (1H, br s, 1-position). **4d**, yield 0.68 g (49%). mp 173 °C. *Anal.* Calcd for $C_{13}H_{10}ClN_3O_2$: C, 56.64; H, 3.66; N, 15.24. Found: C, 56.76; H, 3.59; N, 15.27. ^{1}H-NMR (CD_3COCD_3–D_2O, 400 MHz) δ: 7.25 (2H, br s, aryl H), 7.36 (2H, d, J=9 Hz, 3′- and 5′-positions), 7.64 (2H, br s, aryl H), 8.21 (2H, d, J=9 Hz, 3″- and 5″-positions), 8.43 (1H, br s, 1-position).

Preparation of 1 A hexane solution (4.7 ml) containing 15% *n*-butyllithium was added under ice cooling to a solution of *p*-anisidine (0.62 g, 5 mmol) in 20 ml of THF under N_2. The solution was allowed to stand for 20 min at room temperature, then a solution of **7d** (2.17 g, 5 mmol) in 70 ml of THF was added to the solution under stirring and the mixture was kept for 90 min at room temperature. The mixture was saturated with CO_2, and about 1 ml of H_2O was added. The whole was concentrated under reduced pressure, and ether and 2 N NaOH were added to the residue. The ether layer was extracted twice with 2 N NaOH, and the combined NaOH layer was treated as usual to give 1.05 g (75%) of *N*-tosyl-*p*-chloroaniline. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from petroleum benzin to give 1.07 g (78%) of **1**.

***N*^{1},*N*^{2}-Di(*m*-cyanophenyl)acetamidine** A mixture of *m*-aminobenzonitrile (4.72 g, 0.04 mol), ethyl orthoacetate (3.24 g, 0.02 mol) and AcOH (2.40 g, 0.04 mol) was placed in a flask which was surmounted by a distillation head equipped with a thermometer and condenser. The mixture was heated on an oil bath (bath temperature 130 °C) for 30 min while EtOH formed was distilled off. Further ethyl orthoacetate (6.48 g, 0.04 mol) was added to the mixture, and the whole was heated for an additional 2.5 h under the same conditions. The mixture was concentrated under reduced pressure. The precipitate was collected, washed successively with 7% $NaHCO_3$ and H_2O, and recrystallized from EtOH to give 5.94 g (57%) of *N*^{1},*N*^{2}-di(*m*-cyanophenyl)acetamidine. mp 182—184 °C. *Anal.* Calcd for $C_{16}H_{12}N_4$: C, 73.83; H, 4.65; N, 21.52. Found: C, 74.18; H, 4.60; N, 21.53. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.96 (3H, s, 2-position), 7.14, 7.33, 7.44, 7.87, 8.26 (10H, m, aryl H).

Preparation of 7f Tosyl chloride (1.91 g, 10 mmol) was added to a solution of *N*^{1},*N*^{2}-di(*m*-cyanophenyl)acetamidine (1.82 g, 7 mmol) in 10 ml of anhydrous pyridine. The mixture was allowed to stand for 4 d at room temperature. The precipitate was collected and washed successively with 7% $NaHCO_3$ and H_2O, and recrystallized from EtOH to give 1.97 g (68%) of **7f**. mp 185 °C. *Anal.* Calcd for $C_{23}H_{18}N_4O_2S$: C, 66.65; H, 4.38; N, 13.52. Found: C, 66.56; H, 4.32; N, 13.44. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.73 (3H, s, 2-position), 2.48 (3H, s, tosyl CH_3), 6.68—6.92, 7.33—7.42, 7.58—7.64, 7.73—7.80 (8H, m, aryl H), 7.32 (2H, d, J=9 Hz, 3‴- and 5‴-positions), 7.77 (2H, d, J=9 Hz, 2‴- and 6‴-positions).

Preparation of 8a—f A solution of *p*-nitroaniline (0.69 g, 5 mmol) in 10 ml of anhydrous THF was added to a mixture to *tert*-BuOK (1.68 g, 15 mmol), 12-Crown-4 (0.88 g, 5 mmol) and 30 ml of anhydrous THF with stirring under N_2. The stirring was continued for 30 min at room temperature. A solution of **7** (5.25 mmol) in 30 ml of anhydrous THF was added to the above mixture with stirring, and the whole was allowed to stand for 2 d at room temperature under N_2, then concentrated under reduced pressure. Ether and H_2O were added to the residue, and the ether layer was extracted with 1 N NaOH. The extract was combined with the H_2O layer. The aqueous layer was treated as usual to give *N*-tosylarylamine (from **7a**, 1.31 g, 95%; from **7b**, 1.01 g, 77% from **7c**, 1.22 g, 99%; from **7d**, 1.32 g, 94%; from **7f**, 0.59 g, 44%). The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. A small amount of EtOH was added to the residue, and the precipitate was collected and recrystallized from EtOH to give **8**. The results were as follows: **8a**, yield 1.12 g (79%). mp 120 °C. *Anal.* Calcd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.18; H, 5.30; N, 14.52. ^{1}H-NMR data are given in Table I. **8b**, yield 0.79 g (59%). mp 185 °C. *Anal.* Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.91; H, 5.62; N, 15.63. ^{1}H-NMR (CD_3OD, at −50 °C, 400 MHz) δ: 1.95, 1.98 (3H, s, 2-position of **8b** and **8b′**), 2.28, 2.31 (3H, s, CH_3 of **8b** and **8b′**), 6.69 (d, J=9 Hz, 2″- and 6″-positions of **8b′**), 6.96 (d, J=9 Hz, 2″- and 6″-positions of **8b**), 7.09, 7.10

(d, J=8 Hz, 3′- and 5′-positions of **8b**, and 3″- and 5″-positions of **8b′**), 7.52 (d, J=8 Hz, 2′- and 6′-positions of **8b**), 7.95 (d, J=9 Hz, 2′- and 6′-positions of **8b′**), 8.18 (2H, d, J=9 Hz, 3′- and 5′-positions of **8b** and **8b′**). **8c**, yield 0.97 g (76%). mp 192 °C. *Anal.* Calcd for $C_{14}H_{13}N_3$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.98; H, 5.12; N, 16.41. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.00 (3H, s, 2-position), 7.00—7.50 (7H, m, aryl H), 8.13 (2H, d, J=9 Hz, 3″- and 5″-positions). **8d**, yield 0.85 g (66%). mp 179 °C. *Anal.* Calcd for $C_{14}H_{12}ClN_3$: C, 58.04; H, 4.18; N, 14.50. Found: C, 58.05; H, 4.09; N, 14.64. ^{1}H-NMR (CD_3OD, at −50 °C, 400 MHz) δ: 1.97, 1.98 (3H, s, 2-position of **8d** and **8d′**), 6.80 (d, J=9 Hz, 2″- and 6″-positions of **8d′**), 6.96 (d, J=9 Hz, 2″- and 6″-positions of **8d**), 7.26, 7.28 (d, J=9 Hz, 3′- and 5′-positions of **8d**, and 3″- and 5″-positions of **8d′**), 7.72 (d, J=9 Hz, 2′- and 6′-positions of **8d**), 7.97 (d, J=9 Hz, 2′- and 6′-positions of **8d′**), 8.18, 8.19 (d, J=9 Hz, 3″- and 5″-positions of **8d**, and 3′- and 5′-positions of **8d′**). **8f**, yield 0.55 g (27%). mp 172 °C. *Anal.* Calcd for $C_{15}H_{12}N_4O_2$: C, 64.28; H, 4.32; N, 19.99. Found: C, 64.48; H, 4.26; N, 19.95. ^{1}H-NMR (DMSO-d_6–D_2O, 60 MHz) δ: 2.03 (3H, s, 2-position), 6.83—8.33 (6H, m, aryl H), 8.17 (2H, d, J=9 Hz, 3″- and 5″-positions).

Preparation of 8e *p*-Toluenesulfonic acid monohydrate (0.76 g, 4 mmol) was dried by repeated addition of dry benzene and subsequent evaporation, and was added to a solution of ethyl *N*-(*p*-nitrophenyl)-acetimidate (8.32 g, 0.04 mol) and *m*-chloroaniline (5.10 g, 0.04 mol) in 20 ml of anhydrous benzene. The whole was refluxed for 3 h. The yellow precipitate obtained was filtered off with suction, and the filtrate was extracted with 60 ml of 2 N HCl. The HCl layer was made alkaline with Na_2CO_3, and extracted with ether. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was subjected to column chromatography (Al_2O_3) with benzene–AcOEt (9 : 1) to give crude **8e**. Recrystallization of the crude product from petroleum benzin gave 0.16 g (14%) of pure **8e**. mp 128 °C. *Anal.* Calcd for $C_{14}H_{12}ClN_3O_2$: C, 58.04; H, 4.18; N, 14.50. Found: C, 58.14; H, 4.16; N, 14.42. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.03 (3H, s, 2-position), 7.00—7.50 (6H, m, aryl H), 8.17 (2H, d, J=9 Hz, 3″- and 5″-positions).

Preparation of 8g A mixture of ethyl *N*-(*p*-nitrophenyl)acetimidate (2.04 g, 0.01 mol), *p*-aminobenzonitrile (1.18 g, 0.01 mol), *tert*-BuOK (2.24 g, 0.02 mol) and 80 ml of anhydrous THF was stirred at room temperature for 6 d. The mixture was saturated with CO_2, and the solvent was removed under reduced pressure. A small amount of $CHCl_3$ was added to the residue. The precipitate was collected, washed with water, and recrystallized from EtOH to give 1.10 g (39%) of **8g**. mp 222 °C. *Anal.* Calcd for $C_{15}H_{12}N_4O_2$: C, 64.28; H, 4.32; N, 19.99. Found: C, 63.97; H, 4.56; N, 19.82. ^{1}H-NMR (CD_3OD, at −50 °C, 400 MHz) δ: 2.00, 2.01 (3H, s, 2-position), 6.97 (d, J=9 Hz, 2″- and 6″-positions of **8g′**), 6.98 (d, J=9 Hz, 2″- and 6″-positions of **8g**), 7.64, 7.67, 7.94 (d, J=9 Hz, aryl H of *p*-CNC_6H_4), 7.97 (d, J=9 Hz, 2′- and 6′-positions of **8g′**), 8.20 (d, J=9 Hz, 3′- and 5′-positions of **8g′**), 8.21 (d, J=9 Hz, 3″- and 5″-positions of **8g**).

Preparation of 9a—d 2,4-Dinitroaniline (0.87 g, 4.8 mmol) and **7** (5 mmol) were treated in the same manner as described for the preparation of **8**. The reaction mixture was allowed to stand for 1 d at room temperature, and worked up in the same manner as for the preparation of **8**. The results were as follows: **9a**, yield 0.35 g (21%). mp 169 °C. (EtOH). *Anal.* Calcd for $C_{15}H_{14}N_4O_5$: C, 54.55; H, 4.27; N, 16.96. Found: C, 54.58; H, 4.27; N, 16.93. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 2.04 (3H, s, 2-position), 3.76 (3H, s, OCH_3), 6.84 (2H, d, J=9 Hz, 3′- and 5′-positions), 7.12 (1H, d, J=9 Hz, 6″-position), 7.46 (2H, d, J=9 Hz, 2′- and 6′-positions), 8.33 (1H, dd, J=2, 9 Hz, 5″-position), 8.75 (1H, d, J=2 Hz, 3″-position). **9b**, yield 0.74 g (47%). mp 147 °C (EtOH). *Anal.* Calcd for $C_{15}H_{14}N_4O_4$: C, 57.32; H, 4.49; N, 17.83. Found: C, 57.58; H, 4.47; N, 17.89. ^{1}H-NMR (CD_3OD, 400 MHz) is shown in Table I. ^{1}H-NMR ($CDCl_3$, at −20 °C, 400 MHz) δ: 2.08 and 2.17 (s, 2-position of **9b** and **9b′**), 2.33 and 2.37 (s, aryl CH_3 of **9b** and **9b′**), 6.63 (br s, NH of **9b**), 6.74 (d, J=8 Hz, 2″-position of **9b′**), 7.04 (d, J=9 Hz, 6″-position of **9b**), 7.14 (d, J=8 Hz, 3′- and 5′-positions of **9b**), 7.18 (d, J=8 Hz, 3″- and 5″-positions of **9b′**), 7.38 (d, J=8 Hz, 2′- and 6′-positions of **9b**), 8.33 and 8.43 (each dd, J=2 and 9 Hz, 5″-position of **9b** and 5′-position of **9b′**), 8.89 and 9.22 (each d, J=2 Hz, 3″-position of **9b** and 3′-position of **9b′**), 9.58 (d, J=9 Hz, 6′-position of **9b′**), 10.35 (br s, NH of **9b′**). **9c**, yield 0.98 g (65%). mp 170 °C (EtOH). *Anal.* Calcd for $C_{14}H_{12}N_4O_4$: C, 56.00; H, 4.03; N, 18.66. Found: C, 56.14; H, 3.92; N, 18.67. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 2.06 (3H, s, 2-position), 7.04 (1H, t, J=8 Hz, 4′-position), 7.14 (1H, d, J=9 Hz, 6″-position), 7.26 (2H, t, J=8 Hz, 3′- and 5′-positions), 7.58 (2H, d, J=8 Hz, 2′-and 6′-positions), 8.34 (1H, dd, J=2, 9 Hz, 5″-position), 8.76 (1H, d, J=2 Hz, 3″-position). **9d**, yield 0.97 g (58%). mp 134 °C (EtOH). *Anal.* Calcd for $C_{14}H_{11}ClN_4O_4$: C, 50.24; H, 3.31; N, 16.74. Found: C, 50.30; H, 3.23; N, 16.86. ^{1}H-NMR (CD_3OD, 400 MHz) δ: 2.05 (3H, s, 2-position), 7.15 (1H, d, J=9 Hz, 6″-position), 7.25 (2H, d, J=9 Hz, 3′- and 5′-positions), 7.62 (2H, d, J=9 Hz, 2′- and 6′-positions), 8.35 (1H, dd, J=2, 9 Hz, 5″-position), 8.77 (1H, d, J=2 Hz, 3″-position).

Preparation of 10 and 11 A mixture of acetoxime tosylate (4.55 g, 0.02 mol), an arylamine (0.02 mol) and 60 ml of toluene was refluxed (*p*-nitroaniline, for 40 min; 2,4-dinitroaniline, for 8 h). The precipitate (amidine salt) was collected and washed with acetone. Aqueous Na_2CO_3 and ether were added to the precipitate, and the ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from EtOH to give the corresponding N^1-methyl-N^2-arylacetamidine. The results were as follows: **10**, yield 1.26 g (33%). mp 122 °C. *Anal.* Calcd for $C_9H_{11}N_3O_2$: C, 55.95; H, 5.74; N, 21.75. Found: C, 56.01; H, 5.74; N, 21.74. ^{1}H-NMR data are given in Table I. **11**, yield 3.10 g (65%). mp 129 °C. *Anal.* Calcd for $C_9H_{10}N_4O_4$: C, 45.38; H, 4.23; N, 23.52. Found: C, 45.49; H, 4.18; N, 23.53. ^{1}H-NMR is shown in Table I.

Preparation of 7g by Beckmann Rearrangement A mixture of *p*-nitroacetophenoxime tosylate (16.72 g, 0.05 mol), the sodium salt of *N*-tosyl-*p*-nitroaniline (15.72 g, 0.05 mol) and 200 ml of xylene was refluxed for 4 h. The mixture was filtered with suction, and the precipitate was washed successively with 1 N NaOH and H_2O to give 12.58 g (55%) of crude **7g**. A small amount of the crude sample was recrystallized from EtOH to give pure **7g**. mp 218 °C (dec.). *Anal.* Calcd for $C_{21}H_{18}N_4O_6S \cdot 1/2C_2H_6O$: C, 55.34; H, 4.43; N, 11.73. Found: C, 55.38; H, 4.40; N, 11.68. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.78 (3H, s, 2-position), 2.48 (3H, s, tosyl CH_3), 6.74 (2H, d, J=9 Hz, 2″- and 6″-positions), 7.32 (2H, d, J=9 Hz, 3‴- and 5‴-positions), 7.52 (2H, d, J=9 Hz, 2′- and 6′-positions), 7.76 (2H, d, J=9 Hz, 2‴- and 6‴-positions), 8.19 (2H, d, J=9 Hz, 3″- and 5″-positions), 8.34 (2H, d, J=9 Hz, 3′- and 5′-positions).

N^1-(3,5-Dichlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine Freshly distilled 3,5-dichlorobenzoyl chloride (9.22 g, 0.044 mol) was added to a mixture of **4e** (11.44 g, 0.044 mol), Et_3N (6.06 g, 0.06 mol) and 80 ml of benzene. The whole was refluxed for 30 min on an oil bath. The precipitate was collected, washed successively with 7% $NaHCO_3$ and H_2O, and recrystallized from AcOEt to give 16.04 g (87%) of N^1-(3,5-dichlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine. mp 216 °C. *Anal.* Calcd for $C_{20}H_{12}Cl_2N_4O_5$: C, 52.31; H, 2.63; N, 12.20. Found: C, 52.29; H, 2.64; N, 12.25. ^{1}H-NMR (DMSO-d_6, 60 MHz) δ: 7.23 (2H, d, J=8 Hz, 2″- and 6″-positions), 7.70 (3H, s, 2‴,4‴,6‴-positions), 7.75 (2H, d, J=8 Hz, 2′- and 6′-positions), 8.22 (2H, d, J=9 Hz, 3″- and 5″-positions), 8.30 (2H, d, J=8 Hz, 3′- and 5′-positions), 8.78 (1H, s, 1-position).

Preparation of 12 A mixture of N^1-(3,5-dichlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine (5.51 g, 0.012 mol), *N*-ethyl-*p*-toluidine (1.35 g, 0.01 mol) and 50 ml of toluene was refluxed for 4.5 h on an oil bath. Usual treatment of the precipitate gave 3.42 g (92%) of 3.5-dichloro-4′-nitrobenzanilide. The filtrate was concentrated under reduced pressure, and ether was added to the residue. A small amount of 3,5-dichloro-4′-nitrobenzanilide was precipitated, and was filtered off with suction. The filtrate was concentrated under reduced pressure. The residue was solidified on standing, and was recrystallized from benzene to give 2.55 g (90%) of **12**. mp 77 °C. *Anal.* Calcd for $C_{15}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 67.74; H, 6.06; N, 14.77. ^{1}H-NMR data are presented in the main text.

References

1) M. Sen and J. N. Ray, *J. Chem. Soc.*, **1962**, 647; G. L. Webster and J. S. Rodia, *J. Am. Chem. Soc.*, **75**, 1761 (1953).
2) R. M. Roberts, R. H. DeWolfe, and J. H. Ross, *J. Am. Chem. Soc.*, **73**, 2277 (1951).
3) E. C. Taylor and W. A. Ehrhart, *J. Org. Chem.*, **28**, 1108 (1963).
4) E. S. Hand and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 3505 (1962).
5) L. E. Hinkel, E. E. Ayling, and J. H. Beynon, *J. Chem. Soc.*, **1935**, 1219.
6) J. Oszczapowicz and R. Orlinski, *Rocz. Chem.*, **44**, 2327 (1970); *idem*, *ibid.*, **45**, 103 (1971).
7) J. Oszczapowicz, *Rocz. Chem.*, **44**, 453 (1970).
8) M. Ono and S. Tamura, *Chem. Pharm. Bull.*, **38**, 590 (1990).
9) P. Oxley and W. F. Short, *J. Chem. Soc.*, **1948**, 1514.
10) A. F. Hegarty and A. Chandler, *Tetrahedron Lett.*, **21**, 885 (1980); *idem*, *J. Chem. Soc., Chem. Commun.*, **1980**, 130.
11) D. J. Bertelli and J. T. Gerig, *Tetrahedron Lett.*, **1967**, 2481.
12) D. L. Harris and K. M. Wellman, *Tatrahedron Lett.*, **1968**, 5225.
13) Z. Rappoport and R. Ta-Shma, *Tetrahedron Lett.*, **1972**, 5281.

14) J. Oszczapowicz, E. Raczynska, and J. Osek, *Magn. Reson. Chem.*, **24**, 9 (1986).
15) L. M. Jackman and T. Jen, *J. Am. Chem. Soc.*, **97**, 2811 (1975).
16) J. Oszczapowicz and E. Raczynska, *J. Chem. Soc., Perkin Trans. 2*, **1984**, 1643; E. Raczynska, J. Oszczapowicz, and M. Walczak, *ibid.*, **1985**, 1087; J. Oszczapowicz and K. Ciszkowski, *ibid.*, **1987**, 663.
17) J. A. Gautier, M. Miocque, C. Fauran, and A. Y. Le Cloarec, *Bull. Soc. Chim. Fr.*, **1971**, 478.
18) M. J. Cook, A. R. Katritzky, and S. Nadji, *J. Chem. Soc., Perkin Trans. 2*, **1976**, 211.
19) M. Ono, H. Tanaka, K. Hayakawa, and S. Tamura, *Chem. Pharm. Bull.*, **31**, 3534 (1983).