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Amidines. I. Hydrolysis of N^1-Acyl- and N^1-Tosyl-N^1,N^2-diarylamidines

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In acid hydrolysis of N^1-acyl-N^1,N^2-diarylamidines, a water molecule attacked exclusively the amidine central carbon, and the reaction proceeded in parallel through two pathways. One of them leads to the formation of two *N*-acylarylamines, and the other leads to the formation of *N*,*N*-diacylarylamine and arylamine. Acid hydrolysis of N^1-tosyl-N^1,N^2-diarylamidine was also examined. The results were similar to those of the hydrolysis of N^1-acyl-N^1,N^2-diarylamidines.

Alkaline hydrolysis and alcoholysis of N^1-acyl-N^1,N^2-diarylamidines occurred almost exclusively at the amide carbonyl group to give N^1,N^2-diarylamidines and carboxylic acids or their esters.

The effects of structural change and the aryl substituents on the rate and direction of the reaction were examined.

Keywords *N*-acylacetamidine; *N*-acylformamidine; *N*-tosylacetamidine; *N*-tosylformamidine; hydrolysis; alcoholysis; reaction pathway; structure–reactivity relationship; substituent effect

There are two electrophilic centers in an *N*-acylamidine molecule, *i.e.*, the amide carbonyl and the amidine central carbons. Further, attack of a water molecule as a nucleophile at the latter may proceed *via* two parallel pathways. One of them gives two *N*-acylamines by departure of the acylamino group from the tetrahedral intermediate (pathway a) and the other gives *N*,*N*-diacylamine and amine by departure of the amino group (pathway b). In this paper we will report a study of the acid hydrolysis of N^1-acyl- and N^1-tosyl-N^1,N^2-diarylamidines. Attack of a water molecule took place exclusively at the central carbon of *N*-acyl- and *N*-tosylamidines in the acid hydrolysis, and the resulting intermediate participated in both pathways, a and b, although the former predominated. Alkaline hydrolysis and alcoholysis of *N*-acylamidines occurred at the amide carbonyl group to give amidines and carboxylic acids or their esters (pathway c) with the exception of the case of the alkaline hydrolysis of N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine (**2e**), in which the reaction proceeded mainly through pathway c and in parallel through pathway a to a small extent.

Acid Hydrolysis of N^1-Acyl-N^1,N^2-diarylamidines N^1-(*p*-Chlorobenzoyl)-N^1,N^2-diarylacetamidine (**1**) and N^1-(*p*-chlorobenzoyl)-N^1,N^2-diarylformamidine (**2**) were prepared respectively by the reaction of *p*-chlorobenzoyl chloride with the corresponding N^1,N^2-diarylacetamidine (**3**) and N^1,N^2-diarylformamidine (**4**) in the presence of triethylamine.

N-(*p*-Chlorobenzoyl)-*p*-anisidine (38%), *N*-acetyl-*p*-anisidine (45%), *N*-(*p*-chlorobenzoyl)-*N*-acetyl-*p*-anisidine (9%) and *p*-anisidine (10%) were obtained when a 75% aqueous tetrahydrofuran (THF) solution of N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-methoxyphenyl)acetamidine (**1a**) was kept for 15 min at room temperature in the presence of 2 eq amounts of hydrochloric acid. *p*-Chlorobenzoic acid could not be detected in the reaction mixture. The proportions of *N*-(*p*-chlorobenzoyl)-*p*-anisidine, *N*-acetyl-*p*-anisidine and *N*-(*p*-chlorobenzoyl)-*N*-acetyl-*p*-anisidine formed were evaluated to be 0.85 : 0.79 : 0.18 by integration of the signals of each compound in the ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectrum of the crude products from which *p*-anisidine formed had already been separated. *N*-(*p*-Chlorobenzoyl)-*N*-acetyl-*p*-anisidine showed almost no change on treatment under the same conditions. The results showed that the reaction proceeded in parallel through pathways a and b in a ratio of 4 : 1 (Chart 1). Unchanged starting material (28%) was found by the same analysis when the reaction solution was kept for 2 min under the same conditions. On 5 min standing of the reaction solution, 10% of the starting material remained in the reaction solution. The hydrolysis of N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-chlorophenyl)acetamidine (**1d**) was examined in the same manner. The proportions of *N*-(*p*-chlorobenzoyl)-*p*-chloroaniline, *N*-acetyl-*p*-chloroaniline and *N*-(*p*-chlorobenzoyl)-*N*-acetyl-*p*-chloroaniline formed were evaluated to be 0.95 : 0.94 : 0.05 when a 75% aqueous THF solution of **1d** was kept for 60 min at room temperature in the presence of 2 eq amount of hydrochloric acid. The results showed that the reaction proceeded in parallel through pathways a and b in a ratio of 19 : 1 (Chart 1). Unchanged starting material amounted to 40% when the reaction solution was kept for 15 min under the same conditions.

The results showed that the electron-releasing methoxyl group enhances the reaction rate, and favors pathway b to

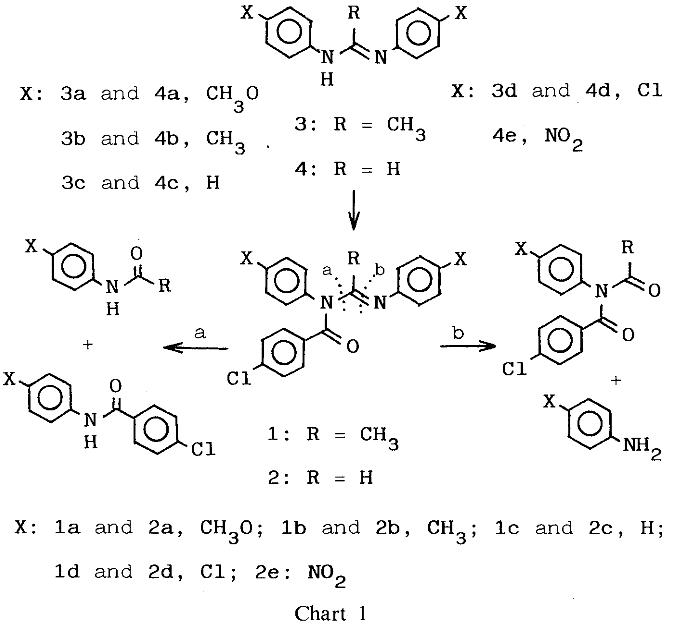

Chart 1

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some extent compared with the chlorine substituent.

DeWolfe and Keefe[1] reported a kinetic study of the acid hydrolysis of N^1,N^2-diarylacetamidine (**3**), and showed that reaction proceeds at measurable rates only at elevated temperature (52.2—100 °C) except for the case of N^1,N^2-di(*p*-nitrophenyl)acetamidine (**3e**), and electron-withdrawing aryl substituents enhance the reaction rate.

Acid hydrolysis of **1** proceeds more easily than that of **3**, and effects of aryl substituents on the reaction rates of the former are opposite to those of the latter. In the acid hydrolysis of **3**, the substrates exist mainly as their conjugate acids, and electron-withdrawing aryl substituents tend to enhance the susceptibility of the amidine central carbon to nucleophilic attack by water. On the other hand, **1** is probably protonated only slightly under the acidic conditions, and electron-withdrawing substituents should diminish the equilibrium concentration of the reactive conjugate acid of **1**, while increasing its susceptibility to nucleophilic attack by water. Probably the former effect is predominant so that electron-withdrawing substituents tend to retard the reaction. The reaction proceeds through a tetrahedral intermediate, and departure of both *N*-(*p*-chlorobenzoyl)arylamino (pathway a) and arylamino (pathway b) groups from the intermediate proceeds with the assistance of acid (Chart 2). Closer approach of the catalytic acid is required for the departure of the arylamino group than that of the *N*-(*p*-chlorobenzoyl)arylamino group. An electron-releasing substituent, *e.g.*, a methoxyl group, enhances the basicity of both nitrogen atoms, but the influence of substituents on the effectiveness of catalytic acid should be greater in relation to the departure of the arylamino group than that of the *N*-(*p*-chlorobenzoyl)-arylamino group.

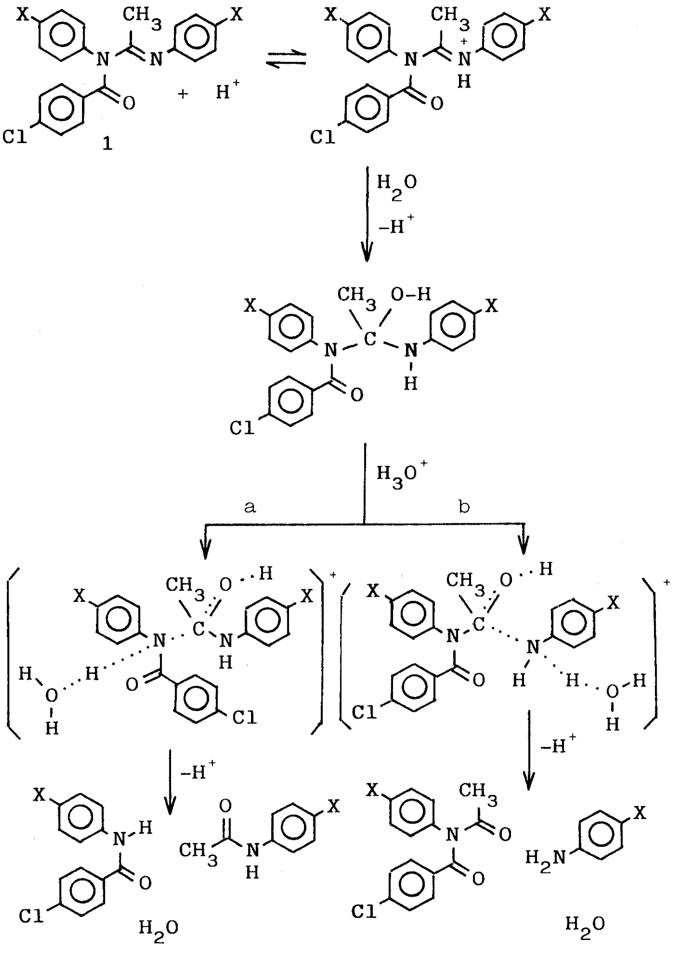


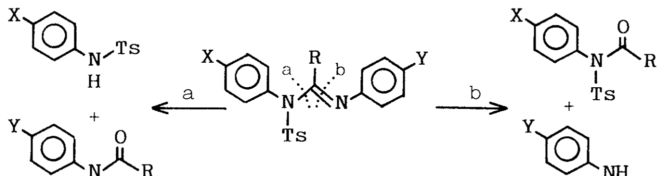
Chart 2

Acid hydrolysis of N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-methoxyphenyl)formamidine (**2a**) and N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-chlorophenyl)formamidine (**2d**) was examined similarly to that of **1a** and **1d**. The reaction was completed within 1 min for both substrates at room temperature. DeWolfe[2] reported that the acid hydrolysis of **4** proceeds much faster than that of **3**, *i.e.*, the reaction proceeds at a measurable rate at 25 °C. The proportions of *N*-(*p*-chlorobenzoyl)-*p*-anisidine (x), *N*-formyl-*p*-anisidine (y) and *N*-(*p*-chlorobenzoyl)-*N*-formyl-*p*-anisidine (z) formed were evaluated to be 0.93 : 0.83 : 0.08 when a 75% aqueous THF solution of **2a** was kept for 5 min at room temperature in the presence of 2 eq amount of hydrochloric acid. Fifteen percent of the starting material was hydrolyzed to give *N*-(*p*-chlorobenzoyl)-*p*-anisidine when *N*-(*p*-chlorobenzoyl)-*N*-formyl-*p*-anisidine was treated under the same conditions. The ratio of pathways a and b is represented by the equation, $a:b=y:(x-y+z)=4:1$. *N*-(*p*-Chlorobenzoyl)-*N*-formyl-*p*-chloroaniline could not be detected in the reaction mixture when **2d** was treated under the same conditions.

Acid Hydrolysis of N^1-Tosyl-N^1,N^2-diarylamidines *N*-Tosyl-*p*-anisidine (69%), *N*-acetyl-*p*-anisidine (48%) and *N*-tosyl-*N*-acetyl-*p*-anisidine (16%) were obtained when an aqueous ethanol solution of N^1-tosyl-N^1,N^2-di(*p*-methoxyphenyl)acetamidine (**5a**) was kept for 30 min at room temperature in the presence of 2 eq amount of hydrochloric acid. The reaction proceeded with greater facility than the alkaline hydrolysis of **5a**, which proceeded only at more elevated temperature.[3]

Acid hydrolysis of **5** proceeds in parallel through pathways a and b (Chart 3). The ratios of pathways a and b were evaluated by a similar method to that used for the acid hydrolysis of **1** and **2**. The results (a : b) were as follows: **5a**, 65 : 35; **5b**, 68 : 32; **5c**, 71 : 29; **5d**, 91 : 9. Electron-releasing aryl substituents tend to favor pathway b.

Oxley and Short[4] prepared N^1-benzenesulfonyl-N^2-methylacetamidine by Beckmann rearrangement of acet-



5: R = CH_3; 6: R = H

5a, X = Y = CH_3O; 5b, X = Y = CH_3; 5c, X = Y = H;
5d, X = Y = Cl; 5e, X = CH_3O, Y = Cl; 5f, X = CH_3;
Y = Cl; 5g, X = H, Y = Cl; 5h, X = NO_2, Y = Cl;
5i, X = Cl, Y = CH_3O
6a, X = Y = CH_3O; 6b, X = Y = CH_3; 6c, X = Y = H;
6d, X = Y = Cl

Chart 3

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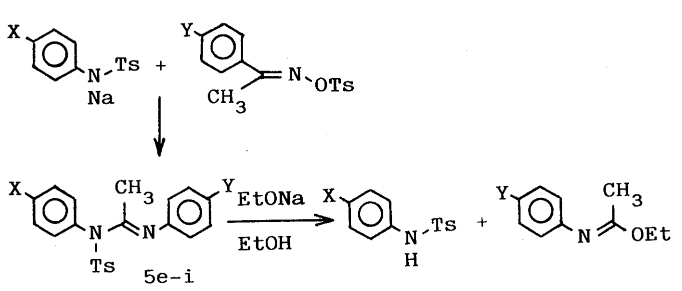

Chart 4

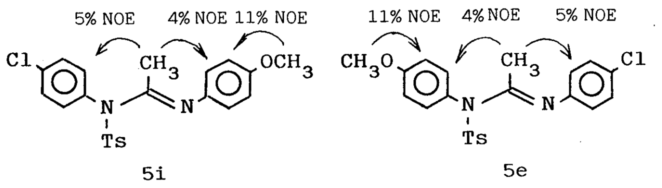

Chart 5

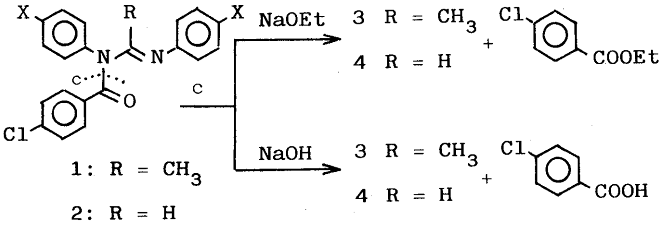

Chart 6

oxime benzenesulfonate in the presence of benzenesulfonamide and pyridine. N^1-Tosyl derivatives of unsymmetrical N^1,N^2-diarylacetamidine were prepared by Beckmann rearrangement of substituted acetophenoxime tosylates in the presence of the sodium salt of *N*-tosylarylamine, *e.g.*, N^1-tosyl-N^1-(*p*-methoxyphenyl)-N^2-(*p*-chlorophenyl)acetamidine (**5e**) was prepared by refluxing a dioxane solution of *p*-chloroacetophenoxime tosylate for 1 h in the presence of the sodium salt of *N*-tosyl-*p*-anisidine. The structure of **5e** was supported by the fact that *N*-tosyl-*p*-anisidine and ethyl *N*-(*p*-chlorophenyl)acetimidate were obtained on refluxing an ethanol solution of **5e** in the presence of sodium ethoxide. The migration of the tosyl group was proved, therefore, not to take place during the Beckmann rearrangement (Chart 4).

Acid hydrolysis of N^1-tosyl derivatives of unsymmetrical diarylacetamidines was examined in the same manner as described above. The ratios of pathways a and b were as follows: **5e**, 70 : 30; **5f**, 77 : 23; **5g**, 87 : 13 and **5h**, 100 : 0. Electron-withdrawing substituents on the N^1-aryl group (X) favor pathway a by increasing the leaving ability of the *N*-tosylarylamino group while electron-releasing substituents on the N^2-aryl group (Y) favor pathway b by increasing the basicity of arylamino nitrogen of the tetrahedral intermediate, so increasing the effectiveness of the catalytic acid.

N^1-Tosyl-N^1-(*p*-chlorophenyl)-N^2-(*p*-methoxyphenyl)-acetamidine (**5i**) was prepared for structural analysis of *N*-tosyldiarylamidines by ^{1}H-NMR. *p*-Methoxyacetophenoxime tosylate is too unstable to isolate from the reaction mixture of *p*-methoxyacetophenoxime and tosyl chloride. The sodium salt of *N*-tosyl-*p*-chloroaniline was added to a THF solution in which *p*-methoxyacetophenoxime, tosyl chloride and triethylamine were dissolved beforehand, and the mixture was refluxed for 2 h to give **5i**. The signals in the ^{1}H-NMR spectra of **5i** and **5e** were assigned by nuclear Overhauser effect (NOE) and internuclear double resonance (INDOR) techniques to show that the signals from *o*-positions with respect to the imino nitrogen (2″- and 6″-positions, Chart 5) are observed at high applied magnetic field (see the Experimental section). Oszczapowicz *et al.*[5] reported that the signals from *o*-positions to the N^2-aryl group are observed at higher applied magnetic field than those from *o*-positions with respect to the N^1-aryl group in the ^{1}H-NMR spectra of trisubstituted amidines.

N^1-Tosyl-N^1,N^2-diarylformamidines (**6**) were prepared by the reaction of **4** and tosyl chloride in the presence of triethylamine. Acid hydrolysis of **6** proceeded faster than that of **5**, *e.g.*, *N*-tosyl-*p*-toluidine and *N*-formyl-*p*-toluidine were obtained when N^1-tosyl-N^1,N^2-di(*p*-methylphenyl)formamidine (**6b**) was dissolved in aqueous ethanol–THF containing hydrochloric acid, and the mixture was neutralized immediately after dissolution. N^1,N^2-Di(*p*-methylphenyl)formamidine (**4b**) could not be detected in the reaction mixture.

Alkaline Hydrolysis and Alcoholysis of N^1-Acyl-N^1,-N^2-diarylamidines Ethyl *p*-chlorobenzoate and **3d** were formed when an ethanol–THF solution of **1d** was kept at room temperature in the presence of sodium ethoxide. The completion of the reaction required 7 h standing of the reaction solution. *N*-(*p*-Chlorobenzoyl)-*p*-chloroaniline could not be detected in the reaction mixture. The reaction proceeded exclusively through pathway c (Chart 6). Electron-releasing aryl substituents tend to retard the reaction. Thus the completion of alcoholysis of **1b** was required warming the ethanol–THF solution of **1b** at 45 °C for 11 h in the presence of sodium ethoxide. Alcoholysis of **2a**—**d** was completed after 1 h standing of an ethanol–THF solution of **2a**—**d** at room temperature in the presence of sodium ethoxide to give **4a**—**d** and ethyl *p*-chlorobenzoate in quantitative yields.

Oszczapowicz *et al.*[6] reported that the dissociation constant of the conjugate acid of N^1,N^2-diarylacetamidine (**3**) is about 15 times larger than that of the corresponding N^1,N^2-diarylformamidine (**4**). The rates of the alkaline hydrolysis of *N*-acetylarylamine[7] and *N*-formylarylamine[8] increase with increasing electron-withdrawing effect of aryl substituents. Thus the alcoholysis of *N*-acyl derivatives of **3** proceeds more slowly than that of *N*-acyl derivatives of **4**.

Alcoholysis of N^1-(*p*-chlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine (**2e**) gave N^1,N^2-di(*p*-nitrophenyl)-formamidine (**4e**) and ethyl *p*-chlorobenzoate as main products in the presence of sodium ethoxide. Small amounts of *N*-(*p*-chlorobenzoyl)-*p*-nitroaniline and ethyl *N*-(*p*-nitrophenyl)formimidate were obtained as minor products from the reaction mixture. Ethoxide ion attacked the amidine central carbon to a small extent. Presumably the electron-withdrawing effect of the two nitro groups increases the electrophilic character of the central carbon to a larger extent than that of the amide carbonyl group.

Alkaline hydrolysis of **2** proceeded more easily than that of **1**. Compounds **4a**—**d** and *p*-chlorobenzoic acid were obtained in quantitative yields on stirring a mixture of a THF solution of **2a**—**d** and an aqueous sodium hydroxide solution for 1—2 h at room temperature. The completion of the alkaline hydrolysis of **1d** required 18 h stirring under the same conditions.

The alkaline hydrolysis of **2e** gave **4e** and *p*-chlorobenzoic acid as main products, and small amounts of *N*-(*p*-chlorobenzoyl)-*p*-nitroaniline, *N*-formyl-*p*-nitroaniline and *p*-nitroaniline were isolated from the reaction mixture as minor products.

N-Acyl derivatives of N^1,N^2-diarylamidine were proved to undergo the alkaline hydrolysis and alcoholysis with greater facility than those of ordinary carboxamides.

It is well known that acetylimidazole, an acyl derivative of cyclic amidine, is hydrolyzed with measurable rates at 25 °C under various conditions.[9] This is one of reasons why imidazole acts as an effective nucleophilic catalyst for the hydrolysis of *p*-nitrophenyl acetate. Jencks[10] pointed out that the reactivity of acetylimidazole can be attributed to its relatively small resonance stabilization compared with ordinary carboxamides.

Experimental

All melting points are uncorrected. ^{1}H-NMR spectra were recorded on JEOL PMX-60 and JEOL GX-400 spectrometers with tetramethylsilane as an internal standard. The following abbreviations are used: singlet (s), doublet (d) and multiplet (m).

Amines, *N*-acylamines, *N*-tosylamines, *N*-tosyl-*N*-acylamines, amidines, imidates, esters and carboxylic acids formed in the hydrolysis or alcoholysis of the substrates were identical with the corresponding authentic samples on the bases of mixed melting point measurement or comparison of infrared (IR) spectra. Compounds **5a**—**d** were prepared as described in a previous paper.[3]

N^1-(*p*-Chlorobenzoyl)-N^1,N^2-diarylacetamidine (1a—d) A solution of *p*-chlorobenzoyl chloride (3.85 g, 0.022 mol) in 10 ml of benzene was added to a solution of **3a**—**d** (0.02 mol) and Et_3N (2.42 g, 0.024 mol) in 20 ml of benzene under ice cooling. The whole was allowed to stand at room temperature for 2 d, then washed with 7% $NaHCO_3$, dried over K_2CO_3 and concentrated under reduced pressure. The residue was recrystallized from benzene (for **1d**) or petroleum benzin (for **1a**—**c**). The results were as follows: **1a**: yield 6.69 g (82%), mp 94 °C. *Anal.* Calcd for $C_{23}H_{21}ClN_2O_3$: C, 67.56; H, 5.18; N, 6.85. Found: C, 67.31; H, 5.08; N, 6.61. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.08 (3H, s, 2-position), 3.76 (3H, s, N^2-aryl CH_3O), 3.78 (3H, s, N^1-aryl CH_3O), 6.48 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 6.80 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 6.89 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.14 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 7.31 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.55 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). Other small signals owing to a conformational isomer were observed. These assignments were confirmed by the following experiments: 11% NOE was observed at the δ 6.80 signal on gated irradiation of the methoxyl signal at δ 3.76, 13% NOE was observed at the δ 6.89 signal on gated irradiation of the methoxyl signal at δ 3.78, and 5% NOE at δ 6.48, 5% NOE at δ 7.14, 4% NOE at δ 7.55 were observed on gated irradiation of the methyl signal at δ 2.08. Spin–spin couplings between the signals at δ 6.80 and 6.48, and δ 7.14 and 6.89, were confirmed by INDOR measurements. As stated in the main text, the signals of hydrogens at *o*-positions with respect to the N^2-aryl group are observed at higher applied magnetic field than those from *o*-positions to the N^1-aryl group. **1b**: yield 5.78 g (77%), mp 116 °C. *Anal.* Calcd for $C_{23}H_{21}ClN_2O$: C, 73.30; H, 5.62; N, 7.43. Found: C, 73.44; H, 5.66; N, 7.35. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.06 (3H, s, 2-position), 2.27 (3H, s, N^2-aryl CH_3), 2.34 (3H, s, N^1-aryl CH_3), 6.44 (2H, d, $J=8$ Hz, 2″- and 6″-positions), 7.05 (2H, d, $J=8$ Hz, 3″- and 5″-positions), 7.11 (2H, d, $J=8$ Hz, 2′- and 6′-positions), 7.18 (2H, d, $J=8$ Hz, 3′- and 5′-positions), 7.32 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.57 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). Other small signals owing to a conformational isomer were observed. **1c**: yield 5.51 g (79%), mp 146 °C (lit.,[11] mp 147 °C). *Anal.* Calcd for $C_{21}H_{17}ClN_2O$: C, 72.31; H, 4.91; N, 8.03. Found: C, 72.26; H, 4.87; N, 8.02. **1d**: yield 7.90 g (72%), mp 147 °C. *Anal.* Calcd for $C_{21}H_{15}Cl_3N_2O$: C, 60.38; H, 3.62; N, 6.71. Found: C, 60.36; H, 3.57; N, 6.76. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.11 (3H, s, 2-position), 6.49 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 7.13 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 7.22 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 7.33 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.34 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.54 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). Other small signals owing to a conformational isomer were observed.

N^1-(*p*-Chlorobenzoyl)-N^1,N^2-diarylformamidine (2a—d) N^1,N^2-Diarylformamidines (**4a**—**d**) were prepared according to Oszczapowicz *et al.*[6] and Walther.[12]

Compounds **4a**—**c** (0.04 mol) were dissolved in CH_2Cl_2 (for **4a**, 140 ml; for **4b**, 40 ml; for **4c**, 40 ml), and Et_3N (0.05 mol) and 1.1 eq freshly distilled *p*-chlorobenzoyl chloride were added to the solution. The whole was allowed to stand for 1.5 h at room temperature. The mixture was washed with 7% $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was recrystallized from benzene. For the preparation of **2d**, benzene (60 ml) was used as a reaction solvent, and crude **2d** was recrystallized from AcOEt. The results were as follows: **2a**: yield 14.54 g (92%), mp 177 °C. *Anal.* Calcd for $C_{22}H_{19}ClN_2O_3$: C, 66.92; H, 4.85; N, 7.09. Found: C, 67.07; H, 4.84; N, 7.04. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 3.77 (6H, s, CH_3O), 8.98 (1H, s, 1-position). **2b**: yield 10.58 g (73%), mp 138 °C. *Anal.* Calcd for $C_{22}H_{19}ClN_2O$: C, 72.82; H, 5.28; N, 7.72. Found: C, 72.84; H, 5.23; N, 7.69. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.33 (6H, s, CH_3), 9.00 (1H, s, 1-position). **2c**: yield 12.07 g (90%), mp 138 °C. *Anal.* Calcd for $C_{20}H_{15}ClN_2O$: C, 71.75; H, 4.52; N, 8.37. Found: C, 72.00; H, 4.56; N, 8.24. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 9.00 (1H, s, 1-position). **3d**: yield 11.46 g (71%), mp 164 °C. *Anal.* Calcd for $C_{20}H_{13}Cl_3N_2O$: C, 59.51; H, 3.25; N, 6.94. Found: C, 59.43; H, 3.18; N, 6.95. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 8.90 (1H, s, 1-position). Signals of aryl protons of **2a**—**d** could not be assigned because of their complexity.

N^1-(*p*-Chlorobenzoyl)-N^1,N^2-di(*p*-nitrophenyl)formamidine (2e) Freshly distilled *p*-chlorobenzoyl chloride (21.00 g, 0.12 mol) was added to a mixture of benzene (300 ml), **4e** (28.62 g, 0.10 mol) and Et_3N (13.16 g, 0.13 mol) at room temperature. The whole was refluxed for 2 h on an oil bath. The deposited precipitate was collected, washed successively with 7% $NaHCO_3$ and H_2O, and recrystallized from benzene to give 38.54 g (91%) of **2e**, mp 202 °C. *Anal.* Calcd for $C_{20}H_{13}ClN_4O_5$: C, 56.55; H, 3.08; N, 13.19. Found: C, 56.87; H, 3.07; N, 13.17. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 7.10 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 7.32 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.42 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions), 7.42 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 8.21 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 8.28 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 8.96 (1H, s, 1-position).

N-(*p*-Chlorobenzoyl)-N-acetyl-*p*-anisidine *p*-Chlorobenzoyl chloride (1.58 g, 9 mmol) was added to a solution of *N*-acetyl-*p*-anisidine (1.65 g, 10 mmol) and Et_3N (1.50 g, 15 mmol) in 20 ml of benzene. The whole was refluxed for 4 h. The precipitate was filtered off with suction, and the filtrate was washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. A small amount of ether was added to the remaining oil, and the deposited precipitate was collected and recrystallized from petroleum benzin to give 0.96 g (35%) of *N*-(*p*-chlorobenzoyl)-*N*-acetyl-*p*-anisidine, mp 76 °C. *Anal.* Calcd for $C_{16}H_{14}ClNO_3$: C, 63.27; H, 4.65; N, 4.61. Found: C, 63.37; H, 4.66; N, 4.66. ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 2.25 (3H, s, CH_3), 3.74 (3H, s, CH_3O), 6.93 (2H, d, $J=9$ Hz, 3- and 5-positions), 7.24 (2H, d, $J=9$ Hz, 2- and 6-positions), 7.45 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.66 (2H, d, $J=9$ Hz, 2′- and 6′-positions).

N-(*p*-Chlorobenzoyl)-*N*-acetyl-*p*-chloroaniline was prepared by a similar method from *N*-acetyl-*p*-chloroaniline (10 mmol). Yield 0.92 g (33%), mp 80 °C. *Anal.* Calcd for $C_{15}H_{11}Cl_2NO_2$: C, 58.46; H, 3.60; N, 4.55. Found: C, 58.52; H, 3.60; N, 4.67. ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 2.29 (3H, s, CH_3), 7.38 (2H, d, $J=9$ Hz, 3- and 5-positions), 7.46 (2H, d, $J=9$ Hz, 2- and 6-positions), 7.47 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.66 (2H, d, $J=9$ Hz, 2′- and 6′-positions).

N-(*p*-Chlorobenzoyl)-N-formyl-*p*-anisidine *p*-Chlorobenzoyl chloride (1.58 g, 9 mmol) was added to a solution of *N*-formyl-*p*-anisidine (1.51 g, 9 mmol) and Et_3N (1.50 g, 15 mmol) in 10 ml of benzene, and the whole was warmed for 2 h at 50 °C. The deposited precipitate was filtered off with suction, and the filtrate was washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. A small amount of ether was added to the residue, and the deposited precipitate was collected and recrystallized from petroleum benzin to give 0.55 g (21%) of *N*-(*p*-chlorobenzoyl)-*N*-formyl-*p*-anisidine, mp 133 °C. *Anal.* Calcd for $C_{15}H_{12}ClNO_3$: C, 62.19; H, 4.18; N, 4.83. Found: C, 62.34; H, 4.14; N, 5.08. ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 3.75 (3H, s, CH_3O), 6.95 (2H, d, $J=9$ Hz, 3- and 5-positions), 7.20 (2H, d, $J=9$ Hz, 2- and 6-

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positions), 7.50 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.62 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 9.26 (1H, s, CHO).

N-(*p*-Chlorobenzoyl)-*N*-formyl-*p*-chloroaniline was prepared by a similar method from *N*-formyl-*p*-chloroaniline (10 mmol). Yield 0.52 g (20%), mp 128 °C. *Anal.* Calcd for $C_{14}H_9Cl_2NO_2$: C, 57.17; H, 3.08; N, 4.76. Found: C, 57.35; H, 3.08; N, 4.90. ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 7.35 (2H, d, $J=9$ Hz, 3- and 5-positions), 7.50 (2H, d, $J=9$ Hz, 2- and 6-positions), 7.54 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.66 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 9.21 (1H, s, CHO).

***p*-Chloroacetophenoxime Tosylate** A solution of TsCl (3.81 g, 0.02 mol) in 2.42 g of Et_3N was added to a solution of *p*-chloroacetophenoxime (3.39 g, 0.02 mol) in 10 ml of ether in portions under ice cooling. The whole was allowed to stand overnight at room temperature, and cooled in an ice bath. The deposited precipitate was collected, and washed successively with H_2O and a small amount of ether. The product was dissolved in a small amount of $CHCl_3$, and petroleum ether was added to the solution. The deposited precipitate was collected to give 3.66 g (57%) of pure *p*-chloroacetophenoxime tosylate, mp 99 °C. *Anal.* Calcd for $C_{15}H_{14}ClNO_3S$: C, 55.64; H, 4.36; N, 4.33. Found: C, 55.26; H, 4.38; N, 4.31. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 2.33 (3H, s, CH_3), 2.47 (3H, s, tosyl CH_3), 7.17—7.62 (6H, m, aryl H), 7.92 (2H, d, $J=9$ Hz, 2′- and 6′-positions).

Acid Hydrolysis of 1a,d Compounds **1a,d** (0.5 mmol) were dissolved in 9 ml of THF, and 1 ml of 1 N HCl and 2 ml of H_2O were added to the solution. The whole was allowed to stand at room temperature (for **1a**, 15 min; for **1d**, 60 min). Ten milliliters of 7% $NaHCO_3$ was added to the mixture, and the mixture was extracted with 10 ml of ether. The ether layer was extracted with 5 ml of 7% $NaHCO_3$. The combined aqueous layer was extracted with 5 ml of ether. No organic material could be detected in the aqueous layer. The combined ether layer was extracted successively with 2 ml and 1 ml of 1 N HCl, and the HCl layer was concentrated under reduced pressure. The residue was treated as usual to give the arylamine. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was subjected to preparative thin layer chromatography (TLC) (silica gel) with $CHCl_3$–ether (4:1) to give *N*-(*p*-chlorobenzoyl)arylamine, *N*-acetylarylamine and *N*-(*p*-chlorobenzoyl)-*N*-acetylarylamine. The results [yields of *N*-(*p*-chlorobenzoyl)arylamine, *N*-acetylarylamine, *N*-(*p*-chlorobenzoyl)-*N*-acetylarylamine and arylamine] were as follows: **1a**: 0.0498 g (38%), 0.0374 g (45%), 0.0132 g (9%), 0.0060 g (10%); **1d**: 0.1020 g (74%), 0.0446 g (51%), could not be isolated, 0.0169 g as hydrochloride (21%).

Acid Hydrolysis of 2a,d Compounds **2a,d** were dissolved in 9 ml of THF, and 1 ml of 1 N HCl and 2 ml of H_2O were added to the solution. The mixture was allowed to stand for 5 min at room temperature. Ten milliliters of 7% $NaHCO_3$ was added to the mixture, and the whole was worked up in the same manner as described in the preceding section. The results [yields of *N*-(*p*-chlorobenzoyl)arylamine, *N*-formylarylamine, *N*-(*p*-chlorobenzoyl)-*N*-formylarylamine and arylamine] were as follows: **2a**: 0.0730 g (56%), 0.0157 g (21%), could not be isolated, 0.0078 g (13%); **2d**: 0.0930 g (70%), 0.0469 g (60%), could not be isolated, 0.0248 g as hydrochloride (30%).

Acid Hydrolysis of *N*-(*p*-Chlorobenzoyl)-*N*-formyl-*p*-anisidine *N*-(*p*-Chlorobenzoyl)-*N*-formyl-*p*-anisidine (0.1433 g, 0.5 mmol) was treated in the same manner as described for the acid hydrolysis of **2a**. *N*-(*p*-Chlorobenzoyl)-*p*-anisidine (0.0069 g, 5%) was isolated from the neutral fraction of the reaction mixture by recrystallization from petroleum benzin. The starting material (0.1043 g, 73%) was recovered from the mother liquor.

N-(*p*-Chlorobenzoyl)arylamine could not be isolated from the reaction mixture in which *N*-(*p*-chlorobenzoyl)-*N*-acetyl-*p*-anisidine or *N*-(*p*-chlorobenzoyl)-*N*-acetyl-*p*-chloroaniline or *N*-(*p*-chlorobenzoyl)-*N*-formyl-*p*-chloroaniline was treated as above. In each case, the starting material was recovered.

***N*^{1}-Tosyl-*N*^{1}-aryl-*N*^{2}-(*p*-chlorophenyl)acetamidine (5e—h)** *p*-Chloroacetophenoxime tosylate (3.24 g, 0.01 mol) was dissolved in 10 ml of anhydrous dioxane, and 0.5 g of K_2CO_3, the Na salt of *N*-tosylarylamine (0.011 mol) and 10 ml of dioxane were added to the solution. The whole was refluxed under stirring for 1 h. The precipitate was filtered off from the hot reaction mixture, and the filtrate was concentrated under reduced pressure. The residue was dissolved in $CHCl_3$, and the solution was washed successively with two portions of 50 ml of 1 N NaOH and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from AcOEt to give pure **5e—h**. The results were as follows: **5e**: yield 2.98 g (69%), mp 156 °C. *Anal.* Calcd for $C_{22}H_{21}ClN_2O_3S$: C, 61.60; H, 4.93; N, 6.53. Found: C, 61.54; H, 4.90; N, 6.57. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.63 (3H, s, 2-position), 2.43 (3H, s, tosyl CH_3), 3.84 (3H, s, CH_3O), 6.57 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 6.94 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.22 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 7.23 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 7.25 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.81 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). **5f**: yield 2.31 g (56%), mp 187 °C. *Anal.* Calcd for $C_{22}H_{21}ClN_2O_2S$: C, 63.99; H, 5.13; N, 6.78. Found: C, 64.00; H, 5.08; N, 6.77. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 1.60 (3H, s, 2-position), 2.37, 2.40 (each 3H, s, aryl CH_3), 6.53 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 7.07—7.33 (8H, m, aryl H), 7.77 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). **5g**: yield 3.82 g (96%), mp 177 °C. *Anal.* Calcd for: $C_{21}H_{19}ClN_2O_2S$: C, 63.23; H, 4.80; N, 7.02. Found: C, 63.19; H, 4.73; N, 6.99. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 1.63 (3H, s, 2-position), 2.42 (3H, s, tosyl CH_3), 6.57 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 7.07—7.60 (9H, m, aryl H), 7.77 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). **5h**: yield 2.91 g (66%), mp 181 °C. *Anal.* Calcd for $C_{21}H_{18}ClN_3O_4S$: C, 56.82; H, 4.09; N, 9.47. Found: C, 56.94; H. 4.02; N, 9.47. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 1.77 (3H, s, 2-position), 2.43 (3H, s, tosyl CH_3), 6.58 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 7.23 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 7.30 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.47 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 7.73 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions), 8.30 (2H, d, $J=9$ Hz, 3′- and 5′-positions).

***N*^{1}-Tosyl-*N*^{1}-(*p*-chlorophenyl)-*N*^{2}-(*p*-methoxyphenyl)acetamidine (5i)** A solution of TsCl (1.91 g, 0.01 mol) in 10 ml of anhydrous THF was added to a solution of *p*-methoxyacetophenoxime (1.65 g, 0.01 mol) and Et_3N (1.01 g, 0.01 mol) in 10 ml of anhydrous THF under ice cooling. The whole was allowed to stand in an ice box for 1 d. The deposited precipitate was filtered off, and the filtrate was added to a mixture of the Na salt of *N*-tosyl-*p*-chloroaniline (3.04 g, 0.01 mol) and 150 ml of anhydrous THF. The mixture was refluxed under stirring for 2 h, and the precipitate was filtered off from the hot mixture. The filtrate was concentrated under reduced pressure. The residue dissolved in $CHCl_3$, and the solution was washed successively with 1 N NaOH and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from AcOEt to give 1.54 g (36%) of **5i**, mp 169 °C. *Anal.* Calcd for $C_{22}H_{21}ClN_2O_3S$: C, 61.60; H, 4.93; N, 6.53. Found: C, 61.64; H, 4.92; N, 6.50. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.69 (3H, s, 2-position), 2.43 (3H, s, tosyl CH_3), 3.78 (3H, s, CH_3O), 6.60 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 6.83 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 7.25 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.26 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 7.41 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.79 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions). For comparison, the ^{1}H-NMR ($CDCl_3$, 400 MHz, δ) of **5a** is presented: 1.66 (3H, s, 2-position), 2.42 (3H, s, tosyl CH_3), 3.77 (3H, s, CH_3O of *N*^{2}-aryl), 3.84 (3H, s, CH_3O of *N*^{1}-aryl), 6.59 (2H, d, $J=9$ Hz, 2″- and 6″-positions), 6.82 (2H, d, $J=9$ Hz, 3″- and 5″-positions), 6.93 (2H, d, $J=9$ Hz, 3′- and 5′-positions), 7.23 (2H, d, $J=9$ Hz, 2′- and 6′-positions), 7.24 (2H, d, $J=9$ Hz, 3‴- and 5‴-positions), 7.83 (2H, d, $J=9$ Hz, 2‴- and 6‴-positions).

Alcoholysis of 5a—i A solution of EtONa (0.02 mol) in 25 ml of anhydrous EtOH was added to a solution of **5a—h** (0.005 mol) in a mixture of 10 ml anhydrous EtOH and 25 ml of anhydrous THF. The whole was refluxed (for **5a,b**, 4 h; for **5c**, 3 h; for **5d—h**, 2 h), and saturated with CO_2. The mixture was concentrated under reduced pressure, and the residue was dissolved in ether and extracted with 1 N NaOH. The NaOH layer was treated as usual to give *N*-tosylarylamine. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was distilled under reduced pressure to give pure ethyl *N*-(*p*-chlorophenyl)acetimidate.[13] The results [yields of ethyl *N*-(*p*-chlorophenyl)acetimidate and *N*-tosylarylamine] were as follows: **5a**: 0.59 g (60%), 1.03 g (74%); **5b**: 0.54 g (61%), 1.00 g (77%); **5c**: 0.53 g (65%), 1.06 g (85%); **5d**: 0.64 g (65%), 1.21 g (86%); **5e**: 0.77 g (78%), 1.23 g (89%); **5f**: 0.73 g (74%), 1.08 g (82%); **5g**: 0.74 g (75%), 1.12 g (91%); **5h**: 0.65 g (66%), 1.17 g (80%). For the alcoholysis of **5i**, 2 mmol of the starting material was used. Refluxing time 3 h. The results were as follows: ethyl *N*-(*p*-methoxyphenyl)acetimidate 0.32 g (83%), *N*-tosyl-*p*-chloroaniline 0.50 g (89%). Ethyl *N*-(*p*-methoxyphenyl)acetimidate was prepared according to DeWolfe[13] by refluxing of a mixture of equimolar amounts of *p*-anisidine and ethyl orthoacetate for 1 h. Yield 79%. bp 144 °C/21 mmHg. Matlin *et al.*[14] reported the preparation and ^{1}H-NMR of ethyl *N*-(*p*-methoxyphenyl)acetimidate, but they did not present analytical data. *Anal.* Calcd for $C_{11}H_{15}NO_2$: C, 69.05; H, 6.88; N, 7.36. Found: C, 69.09; H, 6.85; N, 7.32.

***N*^{1}-Tosyl-*N*^{1},*N*^{2}-diarylformamidine (6a—d)** Compounds **4a—d** (0.02 mol) and Et_3N (2.42 g, 0.024 mol) were dissolved in 65 ml of benzene and a solution of TsCl (4.19 g, 0.022 mol) in 15 ml of benzene was added.

The whole was kept under appropriate conditions: for **6a,b**, overnight at room temperature; for **6c**, 13 h at 60 °C; for **6d**, 8 h at 60 °C. The whole was washed with 7% $NaHCO_3$, dried over K_2CO_3, and concentrated under reduced pressure except for the case of **6c**. The residue was recrystallized from petroleum benzin to give **6a,b,d**. Compound **6c** was deposited from the reaction solution; it was collected and washed successively with 7% $NaHCO_3$ and H_2O, and recrystallized from benzene. The results were as follows: **6a**: yield 6.79 g (83%), mp 104 °C. *Anal.* Calcd for $C_{22}H_{22}N_2O_4S$: C, 64.37; H, 5.40; N, 6.82. Found: C, 64.45; H, 5.48; N, 6.75. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 8.63 (1H, s, 1-position). **6b**: yield 5.77 g (76%), mp 133 °C. *Anal.* Calcd for $C_{22}H_{22}N_2O_2S$: C, 69.81; H, 5.86; N, 7.40. Found: C, 69.85; H, 5.91; N, 7.29. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 8.65 (1H, s, 1-position). **6c**: yield 5.79 g (83%), mp 211 °C. *Anal.* Calcd for $C_{20}H_{18}N_2O_2S$: C, 68.55; H, 5.18; N, 7.99. Found: C, 68.24; H, 5.29; N, 7.95. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 8.72 (1H, s, 1-position). **6d**: yield 5.18 g (62%), mp 181 °C. *Anal.* Calcd for $C_{20}H_{16}Cl_2N_2O_2S$: C, 57.29; H, 3.85; N, 6.68. Found: C, 57.57; H, 3.95; N, 6.51. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ: 8.63 (1H, s, 1-position).

***N*-Acetyl-*N*-tosyl-*p*-nitroaniline** A solution of *N*-tosyl-*p*-nitroaniline (5.84 g, 0.02 mol), 4-(*N*,*N*-dimethylamino)pyridine (4.88 g, 0.04 mol) and Ac_2O (2.04 g, 0.02 mol) in 60 ml of THF was allowed to stand for 2 d at room temperature. The deposited precipitate was collected and washed successively with small amounts of H_2O and THF, and recrystallized from benzene to give 4.20 g (62%) of *N*-acetyl-*N*-tosyl-*p*-nitroaniline, mp 210 °C (dec.). *Anal.* Calcd for $C_{15}H_{14}N_2O_5S$: C, 53.88; H, 4.22; N, 8.38. Found: C, 54.12; H, 4.21; N, 8.34. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.02 (3H, s, acetyl CH_3), 2.48 (3H, s, tosyl CH_3), 7.38 (2H, d, $J=9$ Hz, 3'- and 5'-positions), 7.44 (2H, d, $J=9$ Hz, 2- and 6-positions), 7.87 (2H, d, $J=9$ Hz, 2'- and 6'-positions), 8.35 (2H, d, $J=9$ Hz, 3- and 5-positions).

Acid Hydrolysis of 5a—d Compounds **5a—d** (1 mmol) were dissolved in 70% aqueous EtOH (**5a**, 40 ml; **5b**, 43 ml; **5c**, 50 ml; **5d**, 222 ml), and 2 ml of 1 N HCl was added to the solution. The whole was allowed to stand at room temperature (**5a**, 0.5 h; **5b**, 1 h; **5c**, 2.3 h; **5d**, 19 h). Five milliliters of 7% $NaHCO_3$ was added to the solution, and the mixture was concentrated under reduced pressure. The residue was dissolved in $CHCl_3$ and the solution was extracted with 2 N NaOH. The NaOH layer was treated as usual to give *N*-tosylarylamine. The $CHCl_3$ layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was subjected to preparative TLC (silica gel) with benzene–AcOEt (5 : 1) to give *N*-acetylarylamine and *N*-acetyl-*N*-tosylarylamine. In the case of **5c,d**, *N*-acetyl-*N*-tosylarylamine could not be isolated from the residue. The results (yields of *N*-tosylarylamine, *N*-acetylarylamine and *N*-acetyl-*N*-tosylarylamine) were as follows: **5a**: 0.25 g (88%), 0.12 g (73%), 0.05 g (16%); **5b**: 0.23 g (88%), 0.14 g (94%), 0.03 g (10%); **5c**: 0.19 g (77%), 0.09 g (67%); **5d**: 0.26 g (78%), 0.15 g (83%).

The sample used for products analysis by ^{1}H-NMR was prepared as follows: **5a—c** (1 mmol) was dissolved in a mixture of THF (10 ml), EtOH (28 ml) and H_2O (12 ml). Four milliliters of 1 N HCl was added to the solution. The whole was allowed to stand at room temperature (**5a**, for 0.5 h; **5b**, for 1 h; **5c**, for 2.5 h). Ten milliliters of 7% $NaHCO_3$ was added to the solution, and the mixture was concentrated under reduced pressure. The residue was diossolved in $CHCl_3$, and the solution was washed successively with 7% $NaHCO_3$ and H_2O, and dried over Na_2SO_4. A part of the solution was concentrated, and the residue was subjected to ^{1}H-NMR analysis. Compound **5d** (1 mmol) was dissolved in a mixture of THF (40 ml), EtOH (40 ml) and H_2O (30 ml), and 4 ml of 1 N HCl was added to the solution. The whole was kept for 3 h at 40 °C, then treated as above. The results are given in the main text.

Acid Hydrolysis of 5e—h Compounds **5e—h** (1 mmol) were dissolved in a mixture of THF (40 ml), EtOH (40 ml) and H_2O (30 ml), and 4 ml of 1 N HCl was added to the solution. The whole was allowed to stand for 19.5 h at room temperature (in the case of **5h**, the reaction solution was warmed at 40 °C for 19.5 h). Ten milliliters of 7% $NaHCO_3$ was added to the solution, and the mixture was concentrated under reduced pressure. The distillate, after being made acidic by addition of HCl, was evaporated to dryness, and the residue was treated as usual to give *p*-chloroaniline (0.008 g, 6%) in the case of **5e**. In other cases, *p*-chloroaniline could not be detected in the distillates. The residue was dissolved in 50 ml of $CHCl_3$, and 0.5 ml of the solution was used for ^{1}H-NMR analysis. The remaining $CHCl_3$ solution was extracted with 1 N NaOH, and the NaOH layer was treated as usual to give *N*-tosylarylamine. The $CHCl_3$ layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was treated as usual to give *N*-acetylarylamine. The results (yields of *N*-tosylarylamine and *N*-acetylarylamine) were as follows: **5e**: 0.21 g (76%), 0.13 g (79%); **5f**: 0.19 g (73%), 0.11 g (74%); **5g**: 0.22 g (89%), 0.10 g (59%); **5h**: 0.14 g (48%), 0.12 g (71%). The results of ^{1}H-NMR analysis are given in the main text.

Acid Hydrolysis of *N*-Acetyl-*N*-tosylaniline in the Presence of Aniline *N*-Acetyl-*N*-tosylaniline (0.29 g, 1 mmol) was dissolved in 35 ml of EtOH, and 2 ml of 2 N HCl, aniline (0.09 g, 1 mmol) and 15 ml of H_2O were added to the solution. The whole was allowed to stand for 6 h at room temperature, and 40 ml of 7% $NaHCO_3$ was added to the solution. The mixture was concentrated under reduced pressure. The distillate, after being made acidic by addition of HCl, was evaporated to dryness, and the residue was treated as usual to give recovered aniline (0.07 g, 75%). The residue was dissolved in $CHCl_3$, and the solution was extrated successively with 7% $NaHCO_3$ and 1 N NaOH. AcOH could not be detected in the $NaHCO_3$ layer. The NaOH layer was treated as usual to give *N*-tosylaniline (0.01 g, 4%). The $CHCl_3$ layer was treated as usual to give 0.23 g (79%) of unchanged *N*-acetyl-*N*-tosylaniline.

Acid Hydrolysis of 6a—d Compounds **6a—d** (1 mmol) were dissolved in a mixture of THF (10 ml) and EtOH (28 ml). Four milliliters of 1 N HCl and 12 ml of water were added to the solution. Thirty milliliters of 7% $NaHCO_3$ was added to the solution immediately after the addition of HCl to the solution. The mixture was concentrated under reduced pressure. The distillate, after being made acidic by addition of HCl, was evaporated to dryness, and the remaining amine hydrochloride was treated as usual to give the arylamine. The residue was dissolved in ether, and the solution was extracted with 1 N NaOH. The NaOH layer was treated as usual to give *N*-tosylarylamine. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure to give *N*-formylarylamine. The results (yields of *N*-tosylarylamine, *N*-formylarylamine and arylamine) were as follows: **6a**: 0.23 g (83%); 0.01 g (7%), 0.02 g (16%); **6b**: 0.23 g (89%), 0.10 g (74%), could not be isolated; **6c**: 0.20 g (81%), 0.01 g (7%), could not be isolated; **6d**: 0.24 g (86%), 0.07 g (45%), 0.05 g (39%).

Alcoholysis of 1a—d Compounds **1a—d** (4 mmol) were dissolved in a mixture of anhydrous THF (80 ml) and anhydrous EtOH (88 ml). Freshly prepared 1 N NaOEt solution (1.6 ml) was added to the solution. The whole was allowed to stand at room temperature (for **1c** 4 d; for **1d**, 7.5 h) or was warmed at 45 °C (for **1a**, 5.5 h; for **1b**, 11 h). After saturation with CO_2, the mixture was concentrated under reduced pressure. The residue was dissolved in ether, and the solution was washed with 7% $NaHCO_3$, dried over K_2CO_3, and concentrated under reduced pressure. A small amount of petroleum ether was added to the residue. The deposited precipitate was collected and recrystallized from petroleum benzin to give **3a—d**. The filtrate was concentrated under reduced pressure, and the residue was distilled under reduced pressure to give ethyl *p*-chlorobenzoate. The results (yields of **3a—d** and ethyl *p*-chlorobenzoate) were as follows: **1a**: 0.79 g (73%), 0.49 g (66%); **1b**: 0.61 g (64%), 0.56 g (76%); **1c**: 0.66 g (79%), 0.50 g (68%); **1d**: 0.78 g (70%), 0.54 g (73%).

Alcoholysis of 2a—e Compounds **2a—e** (4 mmol) were dissolved in a mixture of anhydrous THF (80 ml) and anhydrous EtOH (88 ml). Freshly prepared 1 N NaOEt solution (0.8 ml) was added to the solution. The whole was allowed to stand for 1 h at room temperature, then saturated with CO_2.

Work-up for **2a—d**: The mixture was concentrated under reduced pressure, the residue was dissolved in $CHCl_3$, and the solution was washed with $NaHCO_3$, then dried over Na_2SO_4. After the removal of the solvent, a small amount of petroleum ether was added to the residue. The deposited precipitate was collected and recrystallized from petroleum benzin to give **4a—d**. The filtrate was concentrated under reduced pressure, and the residue was distilled under reduced pressure to give ethyl *p*-chlorobenzoate. The results (yields of **4a—e** and ethyl *p*-chlorobenzoate) were as follows: **2a**: 0.85 g (83%), 0.62 g (84%); **2b**: 0.72 g (82%), 0.60 g (81%); **2c**: 0.68 g (87%), 0.61 g (83%); **2d**: 0.95 g (90%), 0.60 g (81%).

Work-up for **2e**: One hundred milliliters of $CHCl_3$ and 50 ml of 7% $NaHCO_3$ were added to the mixture. The deposited precipitate was collected and recrystallized from 2-butanone to give **4e** (0.82 g, 72%). The $CHCl_3$ layer of the filtrate was concentrated under reduced pressure. A small amount of $CHCl_3$ was added to the residue, and the deposited precipitate was collected, and recrystallized from AcOEt to give *N*-(*p*-chlorobenzoyl)-*p*-nitroaniline (0.10 g, 9%). The filtrate was concentrated, and the residue was distilled under reduced pressure to give ethyl *p*-chlorobenzoate (0.52 g, 70%). The remaining material was recrystallized from petroleum ether to give ethyl *N*-(*p*-nitrophenyl)formimidate (0.04 g, 5%), mp 67—69 °C (lit.,[15] mp 67—69 °C).

Alkaline Hydrolysis of 1d Compound **1d** (1.67 g, 4 mmol) was dissolved in 84 ml of THF, and 8 ml of 1 N NaOH and 28 ml of H_2O were added to

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the solution. The milky mixture was stirred for 18 h at room temperature; it became transparent. The mixture was saturated with CO_2, and concentrated under reduced pressure. The residue was dissolved in $CHCl_3$, and the solution was extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was treated as usual to give 0.45 g (72%) of *p*-chlorobenzoic acid. The $CHCl_3$ layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from petroleum benzin to give 0.76 g (68%) of **3d**.

Alkaline Hydrolysis of 2a—e Compounds **2a—e** (4 mmol) were dissolved in 84 ml of THF, and 8 ml of 1 N NaOH and 28 ml of H_2O were added to the solution. The milky mixture was stirred at room temperature (for **2a**, 5 h; for **2b**, 5 h; for **2c**, 2 h; for **2d**, 1 h; for **2e**, 0.5 h); it became transparent.

Work-up for **2a—d**: The mixture was saturated with CO_2, and concentrated under reduced pressure. The residue was dissolved in $CHCl_3$, and the solution was extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was treated as usual to give *p*-chlorobenzoic acid. The $CHCl_3$ layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from petroleum benzin to give **4a—d**. The results (yields of **4a—d** and *p*-chlorobenzoic acid) were as follows: **2a**: 0.86 g (84%), 0.53 g (85%); **2b**: 0.77 g (86%), 0.52 g (83%); **2c**: 0.71 g (90%), 0.53 g (85%); **2d**: 0.93 g (88%), 0.51 g (81%).

Work-up for **2e**: The mixture was saturated with CO_2, and concentrated under reduced pressure, and $CHCl_3$ and 7% $NaHCO_3$ were added to the residue. The deposited precipitate was collected, and recrystallized from 2-butanone to give 0.59 g (52%) of **4e**. The $CHCl_3$ layer of the filtrate was extracted once more with 7% $NaHCO_3$, and the combined $NaHCO_3$ layer was treated as usual to give 0.38 g (61%) of *p*-chlorobenzoic acid. The $CHCl_3$ layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to preparative TLC (silica gel) with benzene–AcOEt (6 : 1) to give *N*-(*p*-chlorobenzoyl)-*p*-nitroaniline (0.12 g, 11%), *N*-formyl-*p*-nitroaniline (0.01 g, 2%) and *p*-nitroaniline (0.09 g, 16%).

Compounds **4a—e** were treated in a similar manner to that described for the alkaline hydrolysis of **2a—e** (at room temperature, stirring time 1 d). The starting materials were recovered almost unchanged in the cases of **4a—d** while *p*-nitroaniline was isolated in 65% yield in the case of **4e**.

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