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Hydrolysis of Acyl Derivatives of N^1,N^2-Diarylamidine. I

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The alkaline hydrolyses of N^1-benzoyl-N^1,N^2-diarylacetamidine (V) and N^1-tosyl-N^1,N^2-diarylacetamidine (IX) were examined. In the hydrolysis of V, hydroxide ion attacked the amide carbonyl carbon to form N^1,N^2-diarylacetamidine and benzoic acid. In the hydrolysis of IX, hydroxide ion attacked the amidine carbon, and elimination of the *N*-tosylarylamino group and arylimino group proceeded in parallel, with that of the latter predominating.

The alcoholysis reaction of V proceeded without any added catalyst, in contrast to the case of 1-(*N*-benzoylarylamino)-3-arylimino-1-propene.

A unique peak corresponding to the loss of 64 mass units (sulfur dioxide) was observed in the mass spectrum of IX.

Keywords——alkaline hydrolysis; alcoholysis; N^1-benzoyl-N^1,N^2-diarylacetamidine; N^1-tosyl-N^1,N^2-diarylacetamidine; 1,1-bis(*N*-benzoylarylamino)ethene; MS

In previous papers[1-4] we reported the hydrolysis and the aminolysis of *N*-acyl derivatives of malonaldehyde dianil. The reaction course was elucidated to be as shown in Chart 1. Alkaline hydrolysis of 1-[*N*-benzoyl-*N*-(*p*-methylphenyl)amino]-3-(*p*-methylphenylimino)-1-propene (I) occurred at the amide carbonyl carbon of I to give 1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (malonaldehyde dianil of *p*-toluidine) (II) and benzoic acid. Hydrochloric acid-catalyzed hydrolysis of I occurred at the 3-position of I to give *β*-(*N*-benzoyl-*p*-toluidino)acrolein (III) and *p*-toluidine. The reaction of I and *p*-toluidine afforded II and *N*-benzoyl-*p*-toluidine, and amine attack was elucidated to occur not at the amide carbon but at the 1-position of I (Chart 1).

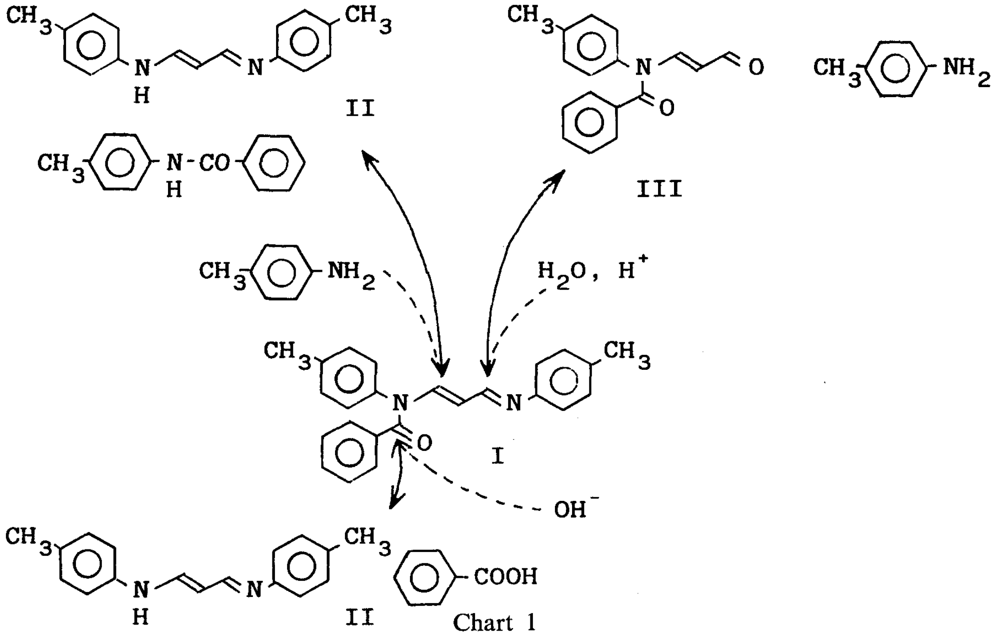
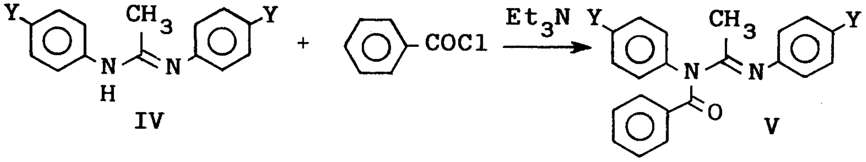


Chart 1

Malonaldehyde dianil can be regarded as a vinylog of N^1,N^2-diarylamidine. For comparison of the regioselectivity of the attacking nucleophilic reagents and leaving tendency of the groups, the hydrolysis of N^1-acyl derivatives of N^1,N^2-diarylacetamidine was examined. In this paper we wish to report alkaline hydrolyses of N^1-benzoyl and N^1-tosyl derivatives of N^1,N^2-diarylacetamidine.

Vigier and Boucherle[5,6] reported the preparation of N^1-aroyl derivatives of N^1,N^2-diarylacetamidine by the reaction of aroyl chloride and amidine in benzene or pyridine solution, while N^1-acetyl derivatives could not be obtained by the reaction of acetyl chloride and amidine under the same conditions. In the latter case, only the *N*-acetyl derivative of the arylamine was obtained.

We have obtained N^1-benzoyl-N^1,N^2-diphenylacetamidine (Vc) in a good yield by the reaction of N^1,N^2-diphenylacetamidine (IVc) and benzoyl chloride in benzene solution in the presence of triethylamine. The melting point of the sample was identical with the value given by Vigier and Boucherle.[5] N^1-Benzoyl-N^1,N^2-bis(*p*-methoxyphenyl)acetamidine (Va) and N^1-benzoyl-N^1,N^2-bis(*p*-methylphenyl)acetamidine (Vb) and N^1-benzoyl-N^1,N^2-bis(*p*-chlorophenyl)acetamidine (Vd) were prepared from the corresponding diarylacetamidines (IVa, IVb and IVd) by the same method. In the reaction of benzoyl chloride and IVa, a prolonged reaction time resulted in a decrease in the yield of Va. A similar tendency was observed in the preparation of Vb.



Y : IVa and Va, CH_3O; IVb and Vb, CH_3
IVc and Vc, H; IVd and Vd, Cl

Chart 2

A mixture of IV and ethyl benzoate was obtained when an ethanolic solution of V was refluxed for 80 min. On the other hand, most of the starting material was recovered when an ethanolic solution of I was refluxed for 80 min. Compound I was methanolyzed to give II and methyl benzoate in the presence of sodium methoxide.[2] The alcoholysis of I proceeds only in the presence of a basic catalyst, while the same reaction of V proceeds without any added catalyst. The alcoholysis of V proceeds even at room temperature. The ^{1}H nuclear magnetic resonance (^{1}H-NMR) spectrum of Va in methanol-d_4 showed signals at δ 2.03 (3H, s, amidine methyl group), 3.73 and 3.82 (each 3H, s, methoxyl groups) immediately after dissolution. At 260 min after dissolution, the signals of Va were smaller, and signals of methyl and methoxyl groups of IVa and of the *ortho*-position of deuteromethyl benzoate were observed at δ 1.90, 3.78 and near δ 8.00, respectively. At 3 d after dissolution, the spectrum showed a pattern identical to that of an equimolar mixture of IVa and deuteromethyl benzoate except for the signal of the methyl group of IVa, which disappeared owing to H-D exchange reaction (Fig. 1, Chart 3).

In order to examine the experimental conditions for alkaline hydrolysis of V, preliminary experiments were carried out as follows. The addition of aqueous sodium hydroxide solution to an aqueous dioxane solution of V caused separation of the reaction solution into two layers. Addition of ethanol to the above mixture gave a homogeneous solution, but the presence of ethanol might lead to alcoholysis of V, complicating the analysis of the reaction products. The alkaline hydrolysis of V was carried out in aqueous acetone solution in the presence of tetramethylammonium hydroxide at 60 °C. The corresponding

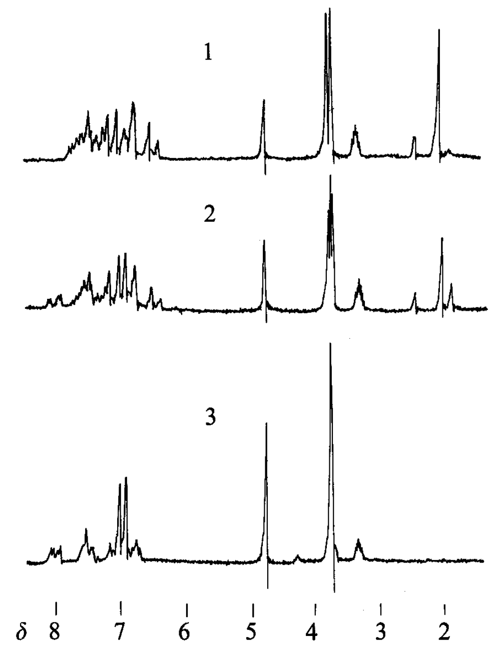


Fig. 1. Changes of the ^{1}H-NMR Spectrum of Va (in CD_3OD)

1: Immediately after dissolution.
2: At 260 min after dissolution.
3: At 3 d after dissolution.

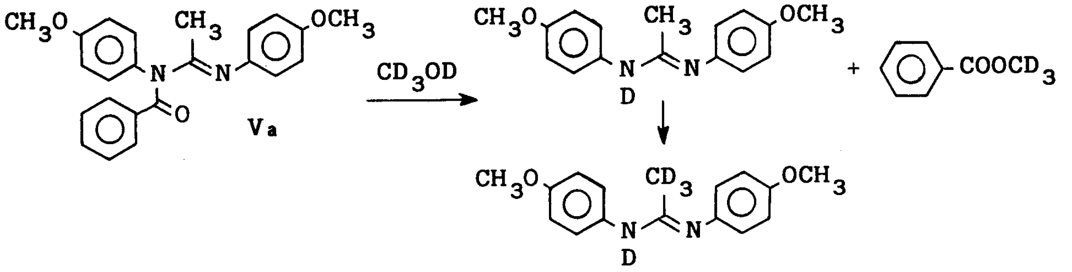


Chart 3

N^1,N^2-diarylacetamidine (IVa—d) and benzoic acid were obtained from the hydrolysis reaction mixture of Va—d in good yields (Chart 4). The result of alkaline hydrolysis of V was similar to that of I, which was hydrolyzed to give II and benzoic acid under similar conditions.[1]

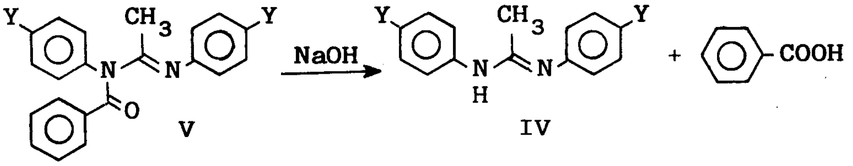


Chart 4

From the hydrolysis reaction mixture of Vb, a small amount of a by-product melting at 240 °C was isolated. The results of elemental analysis were consistent with the values required for the molecular formula $C_{30}H_{26}N_2O_2$. The structure was determined to be 1,1-bis[*N*-benzoyl-*N*-(*p*-methylphenyl)amino]ethene (VIb) by ^{1}H-NMR spectroscopic analysis, *i.e.*, the spectrum (chloroform-*d*) showed signals of methyl groups and of the 2-position at δ 2.27 (6H, s) and 4.72 (2H, s), respectively. Compound VIb was prepared by the reaction of Vb and benzoyl chloride in benzene in the presence of triethylamine.

The possible reaction sequence of alkaline hydrolysis of Vb is shown in Chart 5. Hydroxide ion attacks the amide carbonyl carbon of Vb to form IVb and benzoic acid. At the same time, the nitrogen atom of the conjugate base of Vb, carrying a partial negative charge, attacks the amide carbonyl carbon of Vb to form IVb and VIb. Compound VIb resisted alkaline hydrolysis, in contrast to the case of 1,3-bis[*N*-benzoyl-*N*-(*p*-methylphenyl)amino]-1,3-butadiene (VII), which was hydrolyzed to give 3-[*N*-benzoyl-*N*-(*p*-methylphenyl)amino]-1-(*p*-methylphenylimino)-2-butene (VIII) and benzoic acid under similar conditions[4] (Chart 6). Compound VIb was hydrolyzed to give *N*-benzoyl-*p*-toluidine on being warmed in aqueous dioxane containing hydrochloric acid.

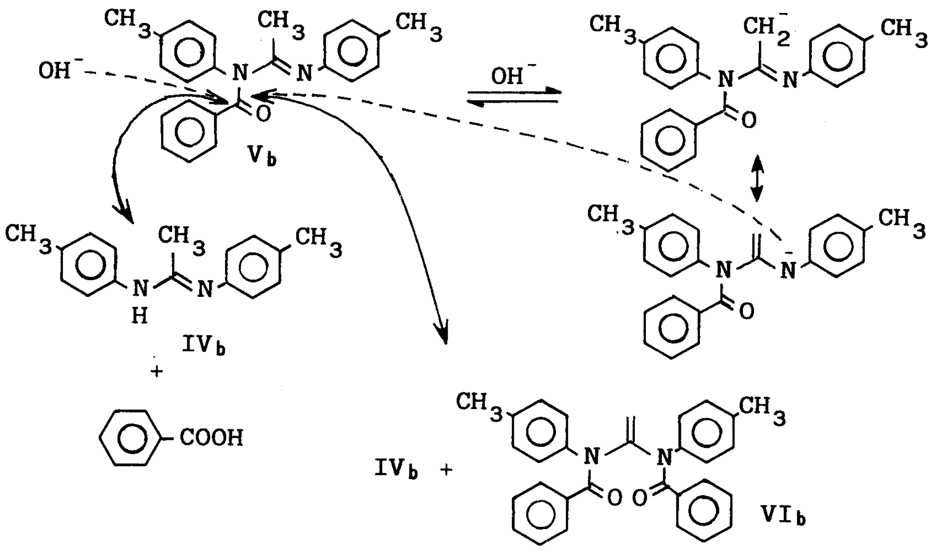


Chart 5

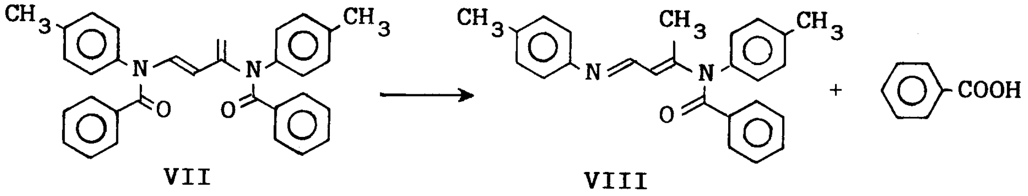


Chart 6

1,1-Bis[*N*-benzoyl-*N*-(*p*-methoxyphenyl)amino]ethene (VIa) was prepared by the same method as used for the preparation of VIb. 1,1-Bis[*N*-benzoyl-*N*-(phenyl)amino]ethene (VIc) and 1,1-bis[*N*-benzoyl-*N*-(*p*-chlorophenyl)amino]ethene (VId) were also prepared by the same method in rather unsatisfactory yields. In the latter cases, most parts of the starting materials (Vc and Vd) were recovered unchanged.

N^1-Tosyl-N^1,N^2-diphenylacetamidine (IXc) was prepared by the reaction of IVc and tosyl chloride in benzene solution in the presence of triethylamine. The melting point of the sample was consistent with the value reported by Vigier and Boucherle.[6] N^1-Tosyl-N^1,N^2-bis(*p*-methoxyphenyl)acetamidine (IXa), N^1-tosyl-N^1,N^2-bis(*p*-methylphenyl)acetamidine (IXb) and N^1-tosyl-N^1,N^2-bis(*p*-chlorophenyl)acetamidine (IXd) were prepared from the corresponding N^1,N^2-diarylacetamidines (IVa, IVb and IVd) by the same method.

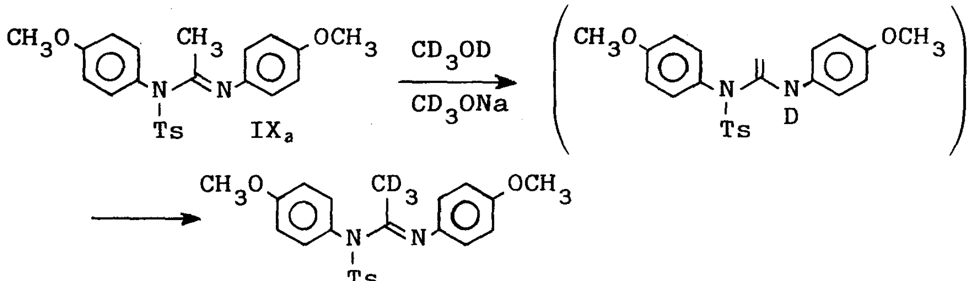
The chemical shifts of amidine methyl signals of IV, V and IX in the ^{1}H-NMR spectra are shown in Table I. The signals of amidine methyl groups of IX were shifted to higher applied field as compared with those of IV and V, presumably owing to the difference of anisotropic effect between the tosyl and benzoyl groups.

Prototropy of IXa was observed by ^{1}H-NMR spectroscopy; this could not be observed in the case of Va owing to the alcoholysis reaction. The spectrum of IXa in methanol-d_4 showed signals at δ 1.60 (3H, s, amidine methyl group) and 2.40 (3H, s, tosyl methyl group). The former signal disappeared at 24 h after the addition of methanol-d_4 containing sodium

TABLE I. ^{1}H-NMR Chemical Shifts of the Amidine Methyl Signals of IV, V and IX (δ in $CDCl_3$)

	a	b	c	d
IV	1.92	1.92	1.95	1.90
V	2.08	2.07	2.08	2.10
IX	1.63	1.60	1.62	1.65

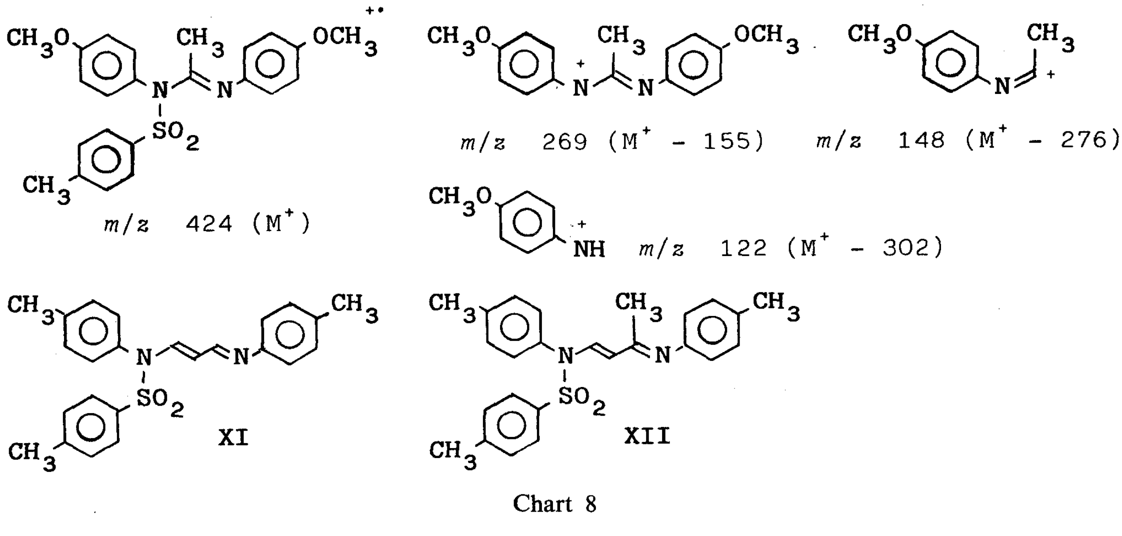
deuteromethoxide (Chart 7). N^1-Tosyl-N^1,N^2-bis(*p*-methoxyphenyl)deuteroacetamidine (X) was prepared by leaving a solution of IXa in methanol-d_4 containing sodium deuteromethoxide to stand for 31 d at room temperature. The mass spectrum (MS) of X showed peaks at *m*/*z* 427 (M^+), 363, 272, 151 and 122. MS of IXa showed peaks at *m*/*z* 424 (M^+), 360, 269, 148 and 122. The peak at *m*/*z* 360 represents the loss of 64 mass units from the molecular ion, which can be attributed to the loss of sulfur dioxide. A metastable peak was observed at *m*/*z* 305. By high-resolution mass measurement (electron impact ionization, 75 eV, three times), the peak of 360 mass units was observed at *m*/*z* 360.1860, 360.1809 and 360.1826 (calculated mass for $C_{23}H_{24}N_2O_2$, 360.1838). The peak of M^+-64 was observed in the MS of IXb, IXc and IXd, while the MS of 1-[*N*-tosyl-*N*-(*p*-methylphenyl)amino]-3-(*p*-methylphenylimino)-1-propene (XI) and 1-[*N*-tosyl-*N*-(*p*-methylphenyl)amino]-3-(*p*-methylphenylimino)-1-butene (XII) did not show a peak of M^+-64 (Chart 8). Grostic[7] observed a peak corresponding to loss of sulfur dioxide in the MS of *N*-tosyl-*N*′-(*n*-butyl)urea.



IXa

X

Chart 7



m/*z* 424 (M^+)

m/*z* 269 (M^+ − 155)

m/*z* 148 (M^+ − 276)

m/*z* 122 (M^+ − 302)

XI

XII

Chart 8

N-Tosylarylamine and *N*-acetylarylamine were obtained when aqueous acetone solutions of IXa—c were refluxed for 2 h in the presence of tetramethylammonium hydroxide, while

64—66% of the starting materials were recovered. The molar ratio of *N*-tosylarylamine and *N*-acetylarylamine formed was about three in each case. For example, in the hydrolysis of IXc, *N*-tosylaniline (21%) and acetanilide (7%) were obtained while 64% of the starting material was recovered. The same reaction of IXd proceeded much faster than those of IXa—c. *N*-Tosyl-*p*-chloroaniline (98%) and *N*-acetyl-*p*-chloroaniline (36%) were obtained when IXd was hydrolyzed under the same conditions, while no starting material could be detected in the reaction mixture. *p*-Toluenesulfonic acid could not be detected in the reaction mixture in any case.

The starting materials (89, 93, 96 and 95%) were recovered when aqueous acetone solutions of *N*-acetyl-*p*-anisidine, *N*-acetyl-*p*-toluidine, acetanilide and *N*-acetyl-*p*-chloroaniline, respectively, were refluxed for 2 h in the presence of tetramethylammonium hydroxide.

N-Tosylaniline and acetic acid were formed when an aqueous ethanolic solution of *N*-tosyl-*N*-acetylaniline[8] was warmed at 40 °C for 2 h in the presence of sodium hydroxide. The aminolysis reaction of *N*-tosyl-*N*-acetylaniline proceeded very slowly. *N*-Tosylaniline and *N*-acetyl-*p*-anisidine were obtained when a dioxane solution of equimolar amounts of *N*-tosyl-*N*-acetylaniline and *p*-anisidine was refluxed for 30 h, while 49% of the *N*-tosyl-*N*-acetylaniline was recovered. *N*-Tosylaniline (50%) and acetanilide (4%) were formed when an aqueous acetone solution of an equimolar mixture of *N*-tosyl-*N*-acetylaniline and aniline was refluxed for 2 h in the presence of tetramethylammonium hydroxide, while 13% of the *N*-tosyl-*N*-acetylaniline was recovered.

In view of these observations, the sequence of alkaline hydrolysis of IX was elucidated to be as shown in Chart 9.

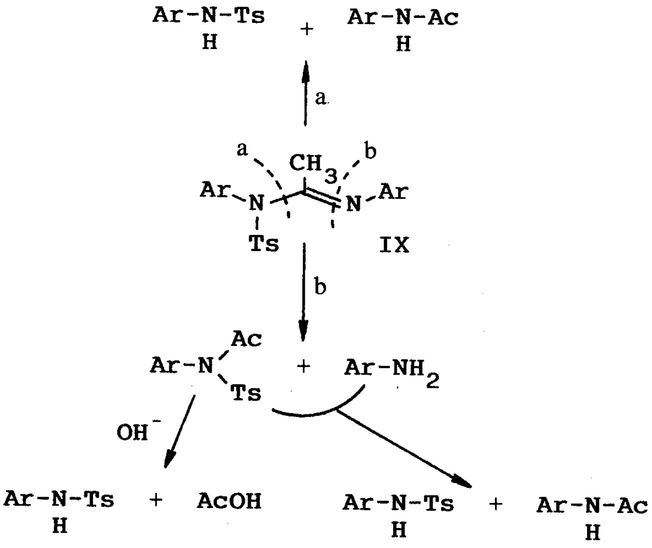


Chart 9

If the reaction proceeds exclusively through course a, equimolar amounts of *N*-tosylarylamine and *N*-acetylarylamine should be formed. Course b seems to account better for the experimental result that a larger amount of *N*-tosylarylamine than *N*-acetylarylamine was formed in the alkaline hydrolysis of IX. The fact that the molar ratio of *N*-tosylaniline and acetanilide formed in the hydrolysis of IXc was about three, however, cannot be explained by course b, because the molar ratio of *N*-tosylaniline and acetanilide formed was more than ten when an equimolar mixture of *N*-tosyl-*N*-acetylaniline and aniline was treated under the same conditions. Course a proceeds, therefore, in parallel with course b to some extent in the alkaline hydrolysis of IX.

Experimental

All melting points are uncorrected. The ^{1}H-NMR spectra were recorded on a JNM-PMX 60 NMR spectrometer with tetramethylsilane as an internal standard. The following abbreviation is used: singlet (s).

The samples of *p*-anisidine, benzoic acid and *n*-acetyl-, *N*-benzoyl- and *N*-tosylarylamines described in this section were identical with the corresponding authentic samples on the bases of mixed melting point measurement and comparison of infrared (IR) spectra. The sample of ethyl benzoate was shown to be identical with an authentic sample by comparison of their IR spectra.

Preparation of N^1,N^2-Diarylacetamidines (IV)——N^1,N^2-Diarylacetamidines were prepared according to Taylor and Ehrhart.[9] The melting points were as follows: IVa, 102 °C; IVb, 123 °C; IVc, 134 °C; IVd, 120 °C.

Preparation of N^1-Benzoyl-N^1,N^2-diarylacetamidines (V)——A benzene solution of IV (0.02 mol), Et_3N (0.04 mol) and BzCl (0.025 mol) was allowed to stand for 1 d at room temperature. The whole was washed with 7% $NaHCO_3$, dried over K_2CO_3 and concentrated under reduced pressure. The residue was recrystallized from an appropriate solvent. The results are shown in Table II.

Preparation of N^1-Tosyl-N^1,N^2-diarylacetamidines (IX)——Compound IV (IVa, 0.019 mol, IVb, 0.021 mol; IVc, 0.024 mol; IVd, 0.018 mol) was dissolved in 50 ml of benzene, and Et_3N (0.04 mol) and 1.1 equivalent of tosyl chloride were added to the solution. The whole was allowed to stand for 2 d at room temperature, then washed with 7% $NaHCO_3$, dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from EtOH. The results are shown in Table III.

Preparation of 1,1-Bis[*N*-benzoyl-*N*-(*p*-methoxyphenyl)amino]ethene (VIa)——Compound Va (1.00 g) was dissolved in 10 ml of benzene, and 0.56 g of Et_3N and 0.47 g of BzCl were added to the solution. The whole was heated at 60 °C for 15 h on a water bath, then washed with 7% $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The product (crude VIa, 0.36 g) was deposited by the addition of a small amount of ether to the residue, and recrystallized from EtOH to give 0.29 g (22%) of pure VIa. mp 220.5 °C. *Anal.* Calcd for $C_{30}H_{26}N_2O_4$: C, 75.30; H, 5.48; N, 5.85. Found: C, 74.78; H, 5.49; N, 5.76. ^{1}H-NMR ($CDCl_3$) δ: 3.75 (6H, CH_3O, s) and 4.73 (2H, CH_2, s).

Preparation of 1,1-Bis[*N*-benzoyl-*N*-(*p*-methylphenyl)amino]ethene (VIb)——Compound Vb (1.50 g) was dis-

Table II. N^1-Benzoyl-N^1, N^2-diarylacetamidines (V)

		Va	Vb	Vc	Vd
mp (°C)		100	132	159[a]	156
Recrystallization solvent		Petroleum benzin	Benzene	Benzene	Benzene
Amount of benzene used for preparation		30 ml	15 ml	50 ml	30 ml
Yield		7.47 g (83%)	5.63 g (82%)	5.46 g (87%)	6.64 g (87%)
Analysis	C	73.78 (73.35)	80.67 (80.79)		65.81 (65.33)
(%)	H	5.92 (5.93)	6.48 (6.58)		4.21 (4.18)
Calcd (Found)	N	7.48 (7.28)	8.18 (8.13)		7.31 (7.05)

[a] Vigier and Boucherle[5] reported the melting point of Vc to be 159 °C.

Table III. N^1-Tosyl-N^1, N^2-diarylacetamidines (IX)

		IXa	IXb	IXc	IXd
mp (°C)		103	107	157[a]	201
Yield		7.85 g (81%)	8.24 g (77%)	8.67 g (72%)	7.75 g (62%)
Analysis (%)	C	65.07 (65.07)	70.38 (70.32)		58.20 (58.31)
	H	5.70 (5.58)	6.16 (6.10)		4.19 (4.07)
Calcd (Found)	N	6.60 (6.51)	7.14 (7.08)		6.46 (6.42)

[a] Vigier and Boucherle[6] reported the melting point of IXc to be 160 °C.

solved in 10 ml of benzene, and 0.90 g of Et_3N and 0.92 g of BzCl were added to the solution. The whole was heated at 60 °C for 15 h on a water bath, then washed with 7% $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The product (crude VIb, 1.37 g) was deposited by the addition of a small amount of ether to the residue, and recrystallized from EtOH to give 1.26 g (64%) of pure VIb. mp 236—240 °C. *Anal.* Calcd for $C_{30}H_{26}N_2O_2$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.70; H, 5.90; N, 6.13.

Preparation of 1,1-Bis(*N*-benzoyl-*N*-phenylamino)ethene (VIc)——Compound Vc (1.00 g) was dissolved in 15 ml of anhydrous benzene, and 0.80 g of Et_3N and 0.66 g of BzCl were added to the solution. The whole was heated at 60 °C for 24 h on a water bath, then washed with 7% $NaHCO_3$, dried over Na_2SO_4 and concentrated under reduced pressure. A small amount of ether was added to the residue. The deposited precipitate was filtered with suction to give 0.70 g (70%) of the starting material (Vc). The filtrate was concentrated under reduced pressure. The residue was recrystallized from EtOH to give 0.055 g (4%) of VIc. mp 165 °C. *Anal.* Calcd for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69. Found: C, 79.75; H, 5.40; N, 6.62. ^{1}H-NMR ($CDCl_3$) δ: 4.75 (2H, CH_2, s). From the mother liquor of recrystallization, a small amount of a by-product melting at 176 °C was obtained. The results of elemental analysis were consistent with the molecular formula $C_{23}H_{20}N_2O$. *Anal.* Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.17; H, 6.00; N, 7.97. The structure has not yet been determined.

Preparation of 1,1-Bis[*N*-benzoyl-*N*-(*p*-chlorophenyl)amino]ethene (VId)——Compound Vd (1.00 g) was dissolved in 15 ml of anhydrous benzene, and 0.52 g of Et_3N and 0.44 g of BzCl were added to the solution. The whole was heated at 60 °C for 24 h on a water bath, then washed with 7% $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. A small amount of ether was added to the residue. The deposited precipitate was filtered with suction to give 0.78 g (78%) of the starting material (Vd). The filtrate was concentrated under reduced pressure and the residue was recrystallized from petroleum benzin to give a trace of VId. mp 236 °C. *Anal.* Calcd for $C_{28}H_{20}Cl_2N_2O_2$: C, 69.00; H, 4.14; N, 5.75. Found: C, 69.29; H, 4.14; N, 5.45. ^{1}H-NMR ($CDCl_3$) δ: 4.67 (2H, CH_2, s).

Treatment of VIb with NaOH——Compound VIb (0.13 g) was dissolved in 7 ml of EtOH, and 3 ml of 1 N NaOH was added to the solution. The whole was refluxed for 1 h, then 5 ml of 7% $NaHCO_3$ was added to the mixture. The mixture was concentrated under reduced pressure and the remaining liquid was extracted with ether. The ether layer was treated as usual to give 0.12 g (92%) of the starting material (VIb). No organic substance could be detected in the $NaHCO_3$ layer.

HCl-Catalyzed Hydrolysis of VIb——Compound VIb (0.45 g) was dissolved in 30 ml of dioxane, and 1 ml of 1 N HCl and 0.5 ml of H_2O were added to the solution. The whole was allowed to stand for 1 d at room temperature, then warmed at 40 °C for 2 h, and 10 ml of 7% $NaHCO_3$ was added to the mixture. The whole was concentrated under reduced pressure. The remaining liquid was extracted with ether. 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 benzene–AcOEt (5 : 1) as a developing solvent to give 0.015 g of the starting material (VIb) and crude *n*-benzoyl-*p*-toluidine. The latter was recrystallized from benzene to give 0.23 g (54%) of pure material.

Treatment of I with EtOH——Compound I (1.06 g) was dissolved in 4 ml of anhydrous tetrahydrofuran (THF), and 50 ml of anhydrous EtOH was added to the solution. The whole was refluxed for 80 min, and concentrated under reduced pressure. The residue was treated as usual to give 0.93 g (88%) of the starting material (I).

Alcoholysis of V——Compound V (0.002 mol) was dissolved in 2 ml of anhydrous THF, and 20 ml of anhydrous EtOH was added to the solution. The whole was refluxed for 80 min, and concentrated under reduced pressure. A small amount of petroleum ether was added to the residue. The deposited precipitate was filtered with suction, and recrystallized from petroleum benzin to give IV. In the case of alcoholysis of Vd, a small amount of the starting material (Vd) was contained in the precipitate, which was subjected to preparative TLC (silica gel) with benzene–AcOEt (4 : 1) as a developing solvent to give IVd and 0.05 g (7%) of Vd. The filtrate was concentrated under reduced pressure and the residue was distilled under reduced pressure to give BzOEt. The yields of IV and BzOEt were as follows. Va: IVa, 0.51 g (94%); BzOEt, 0.21 g (70%). Vb: IVb, 0.39 g (82%); BzOEt, 0.18 g (60%). Vc: IVc, 0.41 g (98%); BzOEt 0.16 g (53%). Vd: IVd, 0.22 g (39%); BzOEt, 0.12 g (40%).

Alkaline Hydrolysis of Va, Vc and Vd——Compound V (0.05 mol) was dissolved in acetone (amount: for Va, 37 ml; for Vc, 50 ml; for Vd, 37 ml), and 6.4 ml of 1.18 M Me_4NOH was added to the solution. Water (amount: for Va, 8.6 ml; for Vc, 16.6 ml; for Vd, 8.6 ml) was added to make the mixture homogeneous. The whole was heated at 65 °C (heating time: for Va, 6 h; for Vc, 7 h; for Vd, 3 h) on a water bath, and 30 ml of 7% $NaHCO_3$ was added. The whole was concentrated under reduced pressure and the remaining liquid was extracted with ether. The ether layer was extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was combined with the above aqueous layer, and the whole was treated as usual to give BzOH. The ether layer was extracted with 0.1 N HCl, and the HCl layer was treated as usual to give IV. No organic substance could be detected in the ether layer. The yields of IV and BzOH were as follows. Va: IVa, 1.13 g (84%); BzOH, 0.33 g (54%). Vc: IVc, 0.88 g (84%); BzOH, 0.44 g (72%). Vd: IVd, 1.24 g (89%); BzOH, 0.41 g (67%).

Alkaline Hydrolysis of Vb——Compound Vb (1.71 g) was dissolved in 40 ml of acetone, and 6.4 ml of 1.18 M Me_4NOH was added to the solution. Water (7.6 ml) was added to the mixture to make the mixture homogeneous. The whole was heated at 65 °C for 6 h on a water bath, and 30 ml of 7% $NaHCO_3$ was added to the mixture. The

TABLE IV. Yields of the Products of Alkaline Hydrolysis of IX[a]

	Recovered IX	*N*-Tosylarylamine	*N*-Acetylarylamine	IV
IXa	0.94 g (66%)	0.10 g (11%)	0.02 g (4%)	
IXb	0.85 g (65%)	0.07 g (8%)	0.01 g (2%)	0.01 g (1%)
IXc	1.16 g (64%)	0.26 g (21%)	0.05 g (7%)	0.05 g (5%)
IXd		0.69 g (98%)	0.15 g (36%)	

a) The amount of the starting material was as follows: IXa, 0.003 mol; IXb, 0.003 mol; IXc, 0.005 mol; IXd, 0.0025 mol.

whole was concentrated under reduced pressure and the remaining liquid was extracted with ether. The ether layer was extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was combined with the above aqueous layer, and the whole was treated as usual to give 0.31 g (51%) of BzOH. The ether layer was extracted with 160 ml of 0.1 N HCl, and the HCl layer was treated as usual to give 1.08 g (91%) of IVb. The ether layer was dried over K_2CO_3, and concentrated under reduced pressure to give 10 mg of VIb.

Alkaline Hydrolysis of IX——Compound IX (IXa, 0.003 mol; IXb, 0.003 mol; IXc, 0.005 mol; IXd, 0.0025 mol) was dissolved in acetone (amount: for IXa, 65 ml; for IXb, 50 ml; for IXc, 110 ml; for IXd, 151 ml), and 1.1 equivalent of 1.18 M Me_4NOH was added to the solution. Water (amount: for IXa, 11 ml; for IXb, 8 ml; for IXc, 18 ml; for IXd, 17 ml) was added to make the mixture homogeneous. The whole was refluxed for 2 h on a water bath, and saturated with CO_2, then concentrated under reduced pressure. The remaining liquid was extracted with $CHCl_3$, and the $CHCl_3$ layer was extracted with 7% $NaHCO_3$. No organic substance could be detected in the aqueous layers. The $CHCl_3$ layer 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. A small amount of ether was added to the residue. The deposited precipitate was subjected to preparative TLC (silica gel) with benzene–AcOEt (5 : 1) as a developing solvent to give *N*-acetylarylamine, IX and IV. The results are shown in Table IV.

Compound IXc (0.004 mol) was dissolved in 200 ml of EtOH, and 4 ml of 1 N NaOH and 46 ml of H_2O were added to the solution. The whole was refluxed for 2 h, then treated as above to give 1.14 g (78%) of IXc, 0.11 g (11%) of *N*-tosylaniline and 0.02 g (4%) of acetanilide.

Compound IXd (0.0025 mol) was dissolved in 20 ml of THF, and 120 ml of EtOH, 2.5 ml of 1 N NaOH and 12.5 ml of H_2O were added to the solution. The whole was refluxed for 40 min, then treated as above to give 0.46 g (43%) of IXd, 0.27 g (39%) of *n*-tosyl-*p*-chloroaniline and 0.04 g (9%) of *N*-acetyl-*p*-chloroaniline.

Treatment of *N*-Acetylarylamine with Me_4NOH——An *N*-acetylarylamine *p*-YC_6H_4NHAc (0.01 mol) was dissolved in acetone (amount: for $Y = CH_3O$, 74 ml; for $Y = CH_3$, 111 ml; for $Y = H$, 108 ml; for $Y = Cl$, 158 ml), and 9.3 ml of 1.18 M Me_4NOH was added to the solution. Water (amount: for $Y = CH_3O$, 14 ml; for $Y = CH_3$, 25 ml; for $Y = H$, 23 ml; for $Y = Cl$, 27 ml) was added to the mixture to make the mixture homogeneous. The whole was refluxed for 2 h, then saturated with CO_2 and concentrated under reduced pressure. The remaining liquid was extracted with ether, and the ether layer was extracted successively with 7% $NaHCO_3$ and 1 N HCl. No organic substance could be detected in the aqueous layers. The ether layer was treated as usual to give the starting material. Amounts of recovered *p*-YC_6H_4NHAc were as follows: $Y = CH_3O$, 1.46 g (89%); $Y = CH_3$, 1.38 g (93%); $Y = H$, 1.30 g (96%); $Y = Cl$, 1.61 g (95%).

Alkaline Hydrolysis of *N*-Tosyl-*N*-acetylaniline——*N*-Tosyl-*N*-acetylaniline (1.00 g) was dissolved in 8 ml of THF, and 40 ml of EtOH, 8.7 ml of 1 N NaOH and 1.4 ml of H_2O were added to the solution. The whole was warmed at 40 °C for 2 h, then saturated with CO_2 and concentrated under reduced pressure. The remaining liquid was extracted with $CHCl_3$. The aqueous layer was treated as usual to give 0.04 g of AcOH. The $CHCl_3$ layer was extracted with 2 N NaOH, and the NaOH layer was treated as usual to give 0.74 g (86%) of *N*-tosylaniline. The $CHCl_3$ layer was treated as usual to give 0.03 g (3%) of the starting material.

Reaction of *N*-Tosyl-*N*-acetylaniline and *p*-Anisidine in Dioxane Solution——*N*-Tosyl-*N*-acetylaniline (0.43 g) and *p*-anisidine (0.19 g) were dissolved in 15 ml of dioxane. The solution was refluxed for 30 h, then 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 0.17 g (46%) of *N*-tosylaniline. The $CHCl_3$ layer was extracted with 1 N HCl, and the HCl layer was treated as usual to give 0.06 g (32%) of *p*-anisidine. The $CHCl_3$ layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was subjected to preparative TLC (silica gel) with benzene–AcOEt (5 : 1) as a developing solvent to give 0.11 g (44%) of *N*-acetyl-*p*-anisidine and 0.21 g (49%) of *N*-tosyl-*N*-acetylaniline.

Reaction of *N*-Tosyl-*N*-acetylaniline and Aniline in Aqueous Acetone Solution in the Presence of Me_4NOH——*N*-Tosyl-*N*-acetylaniline (1.45 g) and aniline (0.47 g) were dissolved in 110 ml of acetone, and 4.8 ml of 1.18 M Me_4NOH and 18 ml of H_2O were added to the solution. The whole was refluxed for 2 h, then 50 ml of 7% $NaHCO_3$ was added to the mixture. The whole was distilled under reduced pressure. The distillate was treated as usual to give 0.20 g (43%)

of aniline. The residue was dissolved in $CHCl_3$, and the $CHCl_3$ solution was extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was treated as usual to give 0.05 g (16%) of AcOH. Both compounds were identified as acetanilide. The $CHCl_3$ layer was extracted with 1 N NaOH, and the NaOH layer was treated as usual to give 0.62 g (50%) of *N*-tosylaniline. The $CHCl_3$ layer was dried over K_2CO_3, and concentrated under reduced pressure. The residue was subjected to preparative TLC (silica gel) with benzene–AcOEt (5 : 1) as a developing solvent to give 0.03 g (4%) of acetanilide and 0.19 g (13%) of *N*-tosyl-*N*-acetylaniline.

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