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Hydrolysis of Acyl Derivatives of Malonaldehyde Dianil. IV.[1] Preparation of β-(*p*-Toluidino)crotonaldehyde

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β-(*p*-Toluidino)crotonaldehyde (V), a possible reactant of the Combes reaction, was prepared by the alkaline hydrolysis of β-*N*-(*p*-chlorobenzoyl)-*p*-toluidinocrotonaldehyde (XXIV). Compound XXIV was prepared by the hydrochloric acid-catalyzed hydrolysis of 3-[*N*-(*p*-chlorobenzoyl)-*p*-methylphenylamino]-1-(*p*-methylphenylimino)-2-butene (XXIII). Compound XXIII was prepared by the alkaline hydrolysis of 1,3-bis[*N*-(*p*-chlorobenzoyl)-*p*-toluidino]-1,3-butadiene (XXII).

The alkaline hydrolysis and alcoholysis of 1,3-bis(*N*-acyl-*p*-toluidino)-1,3-butadiene (VIII) and the hydrochloric acid-catalyzed hydrolysis of 3-(*N*-acyl-*p*-methylphenylamino)-1-(*p*-methylphenylimino)-2-butene (VI) were examined.

Keywords——hydrolysis; β-(*p*-toluidino)crotonaldehyde; β-[*N*-(*p*-chlorobenzoyl)-*p*-toluidino]crotonaldehyde; β-(*N*-tosyl-*p*-toluidino)crotonaldehyde; 3-(*N*-acyl-*p*-methylphenylamino)-1-(*p*-methylphenylimino)-2-butene; 1,3-bis(*N*-acyl-*p*-toluidino)-1,3-butadiene

In previous papers[1-3] we reported the hydrolysis of acyl derivatives of malonaldehyde dianil. Buffer-catalyzed hydrolysis of 1-(*N*-benzoyl-*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (I) occurred at the 3-position of I to form initially β-(*N*-benzoyl-*p*-toluidino)acrolein (II) and *p*-toluidine, and in the next step, aminolysis of II occurred at the

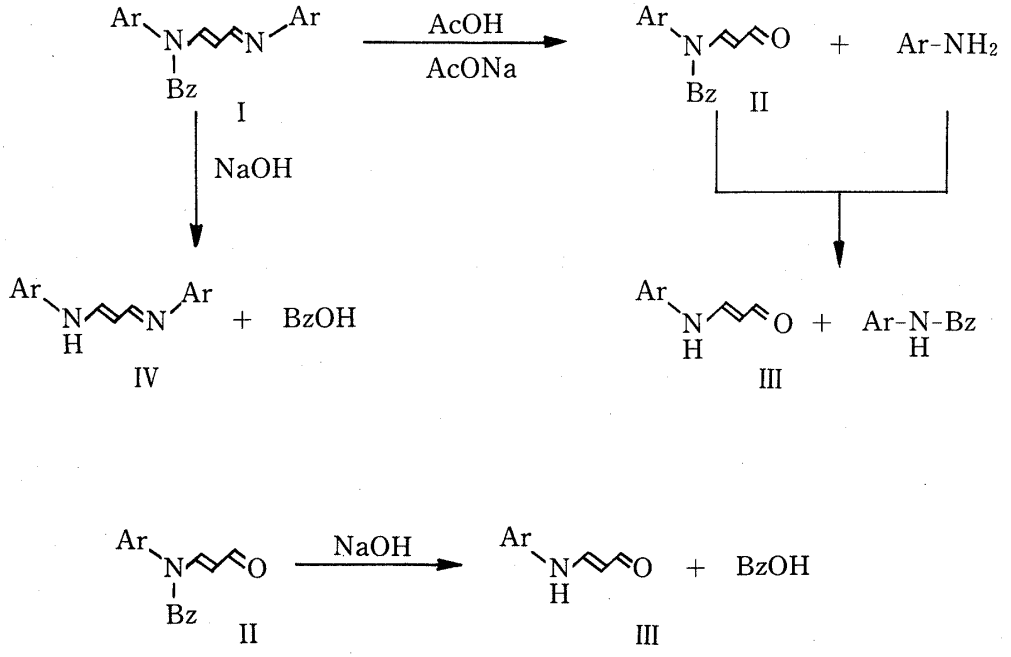
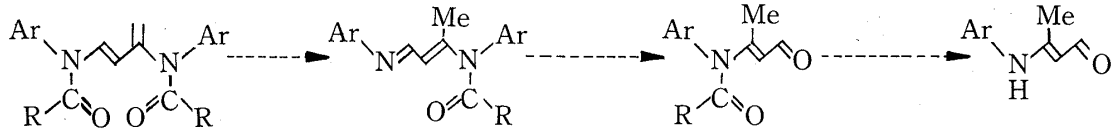


Chart 1

β-position to give β-(*p*-toluidino)acrolein (III) and *N*-benzoyl-*p*-toluidine.[2] Hydrochloric acid-catalyzed hydrolysis of I also occurred at the 3-position of I to give II and *p*-toluidine, but the aminolysis reaction of II was suppressed since most of the *p*-toluidine is converted into unreactive conjugate acid owing to the high acidity of the reaction solution.[1] Alkaline hydrolysis of I afforded 1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (malonaldehyde dianil of *p*-toluidine) (IV) and benzoic acid.[2] Compound II was readily subject to alcoholysis[3] and hydrolysis[1] to form III in the presence of basic catalyst (Chart 1).

In the preceding paper[1] we suggested that it might be possible to prepare β-(*p*-toluidino)-crotonaldehyde (V), a possible reactant of the Combes reaction, *i.e.*, hydrochloric acid-catalyzed hydrolysis of 3-(*N*-acyl-*p*-methylphenylamino)-1-(*p*-methylphenylimino)-2-butene (VI) may afford β-(*N*-acyl-*p*-toluidino)crotonaldehyde (VII), which in turn may afford V on alkaline hydrolysis or alcoholysis.

The preparation of VI from 1,3-bis(*N*-acyl-*p*-toluidino)-1,3-butadiene (VIII) was attempted by elimination of the acyl group of the *N*-acyl-*p*-toluidino group attached at the 1-position of VIII (Chart 2). In a previous paper[2] we reported the preparation of 1,3-bis(*N*-benzoyl-*p*-toluidino)-1,3-butadiene (X) from 1-(*N*-benzoyl-*p*-methylphenylamino)-3-(*p*-meth-



VIII VI VII V

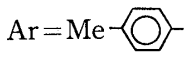
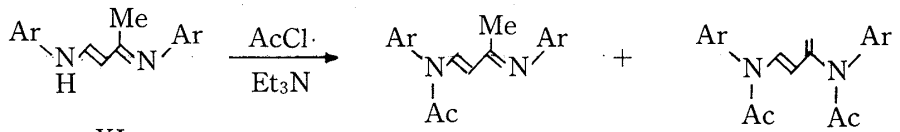
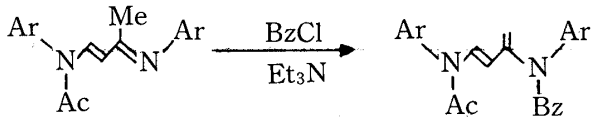


Chart 2

IX X



XI XII XIII



XII XIV

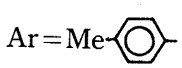


Chart 3

ylphenylimino)-1-butene (IX) and benzoyl chloride. 1-(*N*-Acetyl-*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-butene (XII) and 1,3-bis(*N*-acetyl-*p*-toluidino)-1,3-butadiene (XIII) were obtained when 1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-butene (XI) and acetyl chloride were reacted in the presence of triethylamine. Compound XII could not be crystallized; it was characterized by ^{1}H nuclear magnetic resonance (^{1}H-NMR) spectroscopy. The spectrum (deuterochloroform) showed signals at δ 5.40 (2-position, doublet, J=15 Hz) and 8.37 (1-position, doublet, J=15 Hz). 1-(*N*-Acetyl-*p*-toluidino)-3-(*N*-benzoyl-*p*-toluidino)-1,3-butadiene (XIV) was obtained when XII and benzoyl chloride were reacted in the presence of triethylamine (Chart 3).

Meresaar and Bratt[4] reported that the rate of hydrolysis of acetamide in aqueous sodium hydroxide solution at 45°C is five times faster than that of benzamide. 3-(*N*-Benzoyl-*p*-methylphenylamino)-1-(*p*-methylphenylimino)-2-butene (XV) was obtained when a solution of XIV in aqueous dioxane–methanol was warmed at 40°C for 15 min in the presence of sodium hydroxide. A remarkable amount of XI was formed as a by-product. Shortening of the reaction time resulted in recovery of a large amount of XIV. Compound XII could not be detected in the reaction mixture. Compound XV could not be crystallized; it was characterized by ^{1}H-NMR spectroscopy. The spectrum (deuterochloroform) showed signals at δ 6.28 (2-position, double quartet, J=1, 9 Hz) and 8.37 (1-position, doublet, J=9 Hz), and besides these signals, weak signals of the 2- and 1-positions of the comformational isomer were observed at 6.06 (double quartet, J=1, 9 Hz) and at 8.40 (doublet, J=9 Hz), respectively. Compounds XV and XI and benzoic acid were obtained when a solution of X in aqueous tetrahydrofuran–methanol containing sodium hydroxide was warmed at 40°C for 20 min. The ^{1}H-NMR spectrum of the crude fraction insoluble in aqueous sodium hydrogen carbonate showed a weak singlet signal at δ 3.87, suggesting that a small amount of methyl benzoate was contained in the reaction products. Compound IX could not be detected in the reaction mixture. The course of preparation of XV from XIV has no particular advantage over that from X.

β-(*N*-Benzoyl-*p*-toluidino)crotonaldehyde (XVI), XI, *p*-toluidine and benzoic acid were obtained when a solution of XV in tetrahydrofuran was added to 0.05 N hydrochloric acid with stirring, ether was added to the mixture and the mixture was stirred for 20 min at room temperature. Compound XVI could not be crystallized; it was characterized by ^{1}H-NMR spectroscopy. The spectrum (deuterochloroform) showed signals at δ 5.53 (α-position, double quartet, J=1, 8 Hz) and 9.98 (aldehyde, doublet, J=8 Hz). The ^{1}H-NMR spectrum of the fraction of the reaction product soluble in aqueous hydrochloric acid showed signals due to XI and *p*-toluidine. The molar ratio of XI and *p*-toluidine in the mixture was evaluated by the least-squares method based on the integrated intensities of the signals at δ 1.90—2.40 (methyl groups), 5.00 (2-position of XI) and 6.50—7.50 (aromatic protons) and a value of *p*-toluidine: XI=2: 1 was obtained. In the hydrochloric acid-catalyzed reaction of XV, hydrolysis at the 1-position and the amide carbonyl group proceeded in parallel, in contrast to the same reaction of I, in which hydrolysis occurred only at the 3-position.[1]

1-(*N*-Benzoyl-*p*-toluidino)-3-(*N*-tosyl-*p*-toluidino)-1,3-butadiene (XVII) was prepared from IX and *p*-toluenesulfonyl chloride in the presence of triethylamine. 3-(*N*-Tosyl-*p*-methylphenylamino)-1-(*p*-methylphenylimino)-2-butene (XVIII), benzoic acid and *N*-tosyl-*p*-toluidine were obtained when a solution of XVII in aqueous tetrahydrofuran–methanol containing sodium hydroxide was warmed at 40°C for 20 min. Compound XVIII could not be crystallized. The hydrochloride of XVIII, mp 153°C, was obtained by saturation of the ether solution of XVIII with dry hydrogen chloride. β-(*N*-Tosyl-*p*-toluidino)crotonaldehyde (XIX), *p*-toluidine and *N*-tosyl-*p*-toluidine were obtained when a solution of the hydrochloride of XVIII in methanol was added to 0.1 N hydrochloric acid with stirring, then ether was added and the whole was stirred for 50 min at room temperature. The reaction of β-(*N*-tosyl-*p*-toluidino)acrolein (XX) and *p*-toluidine was examined as a model experiment for the aminolysis

of XIX. The ^{1}H-NMR spectrum (methanol-d_4) of XX showed signals at δ 8.75 (β-position, doublet, J=14 Hz) and 9.42 (aldehyde, doublet, J=8 Hz). At 250 min after the addition of an equimolar amount of *p*-toluidine, signals of IV were observed at δ 5.85 (2-position, triplet, J=10 Hz) and 7.92 (1- and 3-position, doublet, J=10 Hz) and a weak signal (doublet, J=9 Hz) of the formyl group of III was observed at δ 9.15. After 2 days, signals of XX had disappeared, and besides the signals of IV, signals of III were observed at δ 5.63 (α-position, double doublet, J=9, 13 Hz), 7.97 (β-position, doublet, J=13 Hz) and 9.15 (aldehyde, doublet, J=9 Hz). Compound IV, *N*-tosyl-*p*-toluidine and a small amount of III were obtained when XX and *p*-toluidine were reacted in tetrahydrofuran in the presence of *n*-butyllithium. Thus, the aminolysis of XX at the β-position was observed. As reported previously[1] alkaline hydrolysis of XX gave only *N*-tosyl-*p*-toluidine. Compound XIX was hydrolyzed to form *N*-tosyl-*p*-toluidine when a solution of XIX in aqueous methanol containing sodium hydroxide was allowed to stand for one day at room temperature. The ^{1}H-NMR spectrum of XIX in methanol-d_4 showed no change except for H–D exchange at the α-position and methyl group at the β-position of XIX in the presence of triethylamine. Only *N*-tosyl-*p*-toluidine was obtained when XIX and *p*-toluidine were reacted in tetrahydrofuran in the presence of *n*-butyllithium. The ^{1}H-NMR spectrum of an equimolar mixture of XIX and *p*-toluidine in methanol-d_4 showed signals of XIX at δ 5.87 (α-position, doublet, J=8 Hz) and 9.72 (aldehyde,

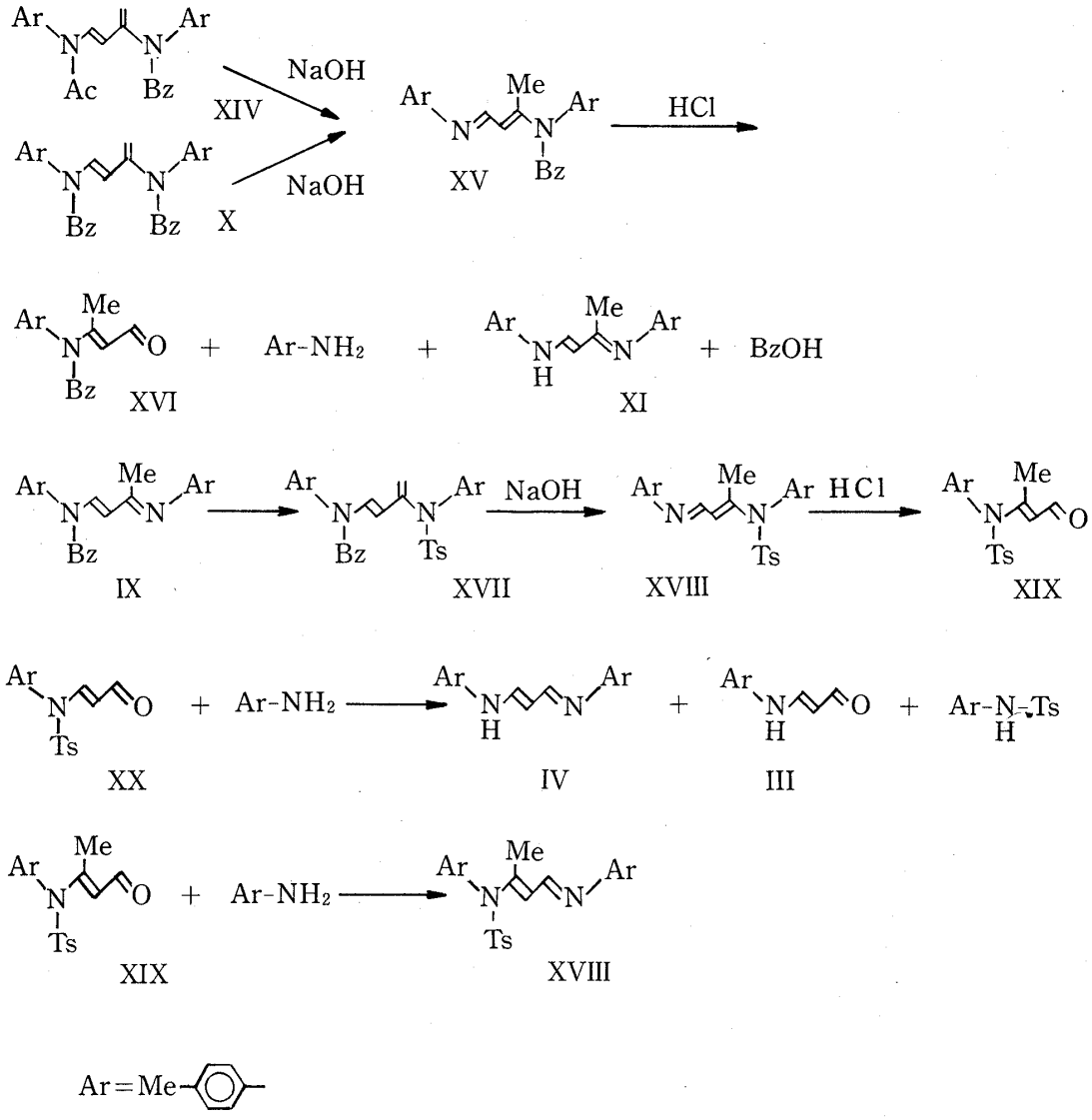


Chart 4

doublet, J=8 Hz) immediately after dissolution. After one day, singals of XIX had disappeared and signals of XVIII were observed at δ 6.42 (2-position, double quartet, J=1, 9 Hz) and 8.43 (1-position, doublet, J=9 Hz). Thus, no evidence for the aminolysis of XIX at its β-position was obtained under the above conditions.

As stated in the former part of this report, in the hydrochloric acid-catalyzed reaction of XV, hydrolysis at the amide carbonyl group proceeded to a marked extent in parallel with that at the 1-position of XV. Meloche and Laidler[5] examined the effect of substituents of the aroyl group on the rate of alkaline and acid hydrolysis of benzamide derivatives, and reported that Hammett's ρ values were 0.7 and −0.15, respectively. 1-[*N*-(*p*-Chlorobenzoyl)-*p*-methylphenylamino]-3-(*p*-methylphenylimino)-1-butene (XXI) was prepared by the reaction of the hydrochloride of XI and *p*-chlorobenzoyl chloride in the presence of triethylamine. 1,3-Bis[*N*-(*p*-chlorobenzoyl)-*p*-toluidino]-1,3-butadiene (XXII) was prepared by the reaction of XXI and *p*-chlorobenzoyl chloride in the presence of triethylamine. 3-[*N*-(*p*-Chlorobenzoyl)-*p*-methylphenylamino]-1-(*p*-methylphenylimino)-2-butene (XXIII), *p*-chlorobenzoic acid and *N*-(*p*-chlorobenzoyl)-*p*-toluidine were obtained when a solution of XXII in aqueous tetrahydrofuran–methanol containing sodium hydroxide was warmed at 40°C for 10 min. The ^{1}H-NMR spectrum of the crude fraction insoluble in aqueous sodium hydrogen carbonate showed a singlet signal at δ 3.83, suggesting that methyl *p*-chlorobenzoate was contained in the reaction products. Compound XXIII could not be crystallized; it was characterized by ^{1}H-NMR spectroscopy. The spectrum (deuterochloroform) showed signals at δ 6.37 (2-position, double quartet, J=1, 9 Hz) and 8.30 (1-position, doublet, J=9 Hz). Besides these signals, weak signals due to the conformational isomer were observed at δ 6.05 (2-position, double quartet, J=1, 9 Hz) and 8.40 (1-position, doublet, J=9 Hz). Alkaline hydrolysis of XXII in non-alcoholic solution was attempted to avoid the formation of methyl *p*-chlorobenzoate, which cannot be separeted from XXIII other than by column chromatography. Compound XXIII and *p*-chlorobenzoic acid were obtained when a solution of XXII in aqueous acetone containing tetramethylammonium hydroxide was warmed at 45°C for 120 min. β-[*N*-(*p*-Chlorobenzoyl)-*p*-toluidino]crotonaldehyde (XXIV), XI, and *p*-toluidine were obtained when a solution of XXIII in tetrahydrofuran was added to 0.05 N hydrochloric acid with stirring, then ether was added and the mixture was stirred for 20 min at room temperature. The molar ratio of *p*-toluidine and XI formed was evaluated as described in the former part of this report and a value of *p*-toluidine: XI=5: 1 was obtained. Compound XXIV could not be crystallized; it was characterized by ^{1}H-NMR spectroscopy. The spectrum (deuterochloroform) showed signals at δ 5.52 (α-position, double quartet, J=1, 8 Hz) and 10.02 (aldehyde, doublet, J=8 Hz). Compound V and *p*-chlorobenzoic acid were obtained when a solution of XXIV in aqueous methanol containing sodium hydroxide was allowed to stand overnight at room temperature (Chart 5).

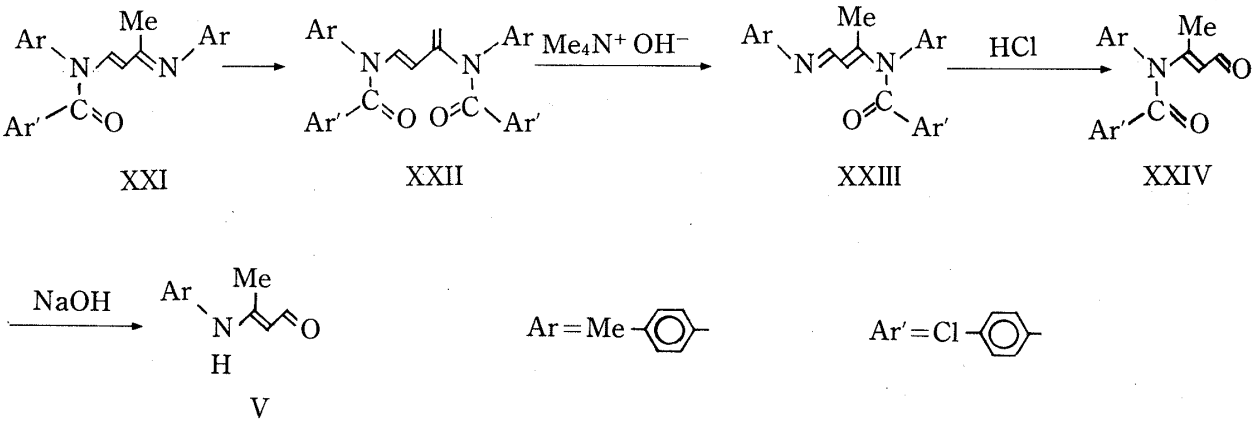


Chart 5

It seems reasonable that the introduction of a strong electron-withdrawing substituent on the aroyl group of VI would suppress the hydrochloric acid-catalyzed hydrolysis of aroylamino group of VI (Chart 2). 1-[*N*-(*p*-Nitrobenzoyl)-*p*-methylphenylamino]-3-(*p*-methylphenylimino)-1-butene (XXV) was prepared by the reaction of the hydrochloride of XI and *p*-nitrobenzoyl chloride in the presence of triethylamine. 1,3-Bis[*N*-(*p*-nitrobenzoyl)-*p*-toluidino]-1,3-butadiene (XXVI) was prepared by the reaction of XXV and *p*-nitrobenzoyl chloride in the presence of triethylamine (Chart 6). Alkaline hydrolysis of XXVI, however, could not be achieved owing to the low solubility of XXVI in the solvents examined.

The base-catalyzed alcoholysis of VIII was also examined. Compound XXIII and methyl *p*-chlorobenzoate were obtained when a solution of XXII in tetrahydrofuran–methanol containing sodium methoxide was allowed to stand for 8 min at room temperature. Compound XVIII, methyl benzoate and *N*-tosyl-*p*-toluidine were obtained when a solution of XVII in tetrahydrofuran–methanol containing sodium methoxide was allowed to stand for 47 min at room temperature. Compound XV and methyl benzoate were obtained when a solution of X in tetrahydrofuran–methanol containing sodium methoxide was allowed to stand for 30 min at room temperature. A large amount of the starting material was recovered from the above reaction mixture. Compound IX was completely alcoholyzed to give XI and methyl benzoate within 6 min under the same conditions. 1-(*N*-Tosyl-*p*-toluidino)-3-(*N*-benzoyl-*p*-toluidino)-1,3-butadiene (XXVIII) was prepared by the reaction of 1-(*N*-tosyl-*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-butene (XXVII) and benzoyl chloride in the presence of triethylamine. The starting material was recovered unchanged when a solution of XXVIII in tetrahydrofuran–methanol containing sodium methoxide was allowed to stand for one day at room temperature. From the above observations it was concluded that the susceptibility of acyl groups to base-catalyzed alcoholysis is in the following order: the acyl group of 1-(*N*-acyl-*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-butene>the acyl group of the *N*-acyl-*p*-toluidino group at the 1-position of VIII>the acyl group of VI, and the acyl group

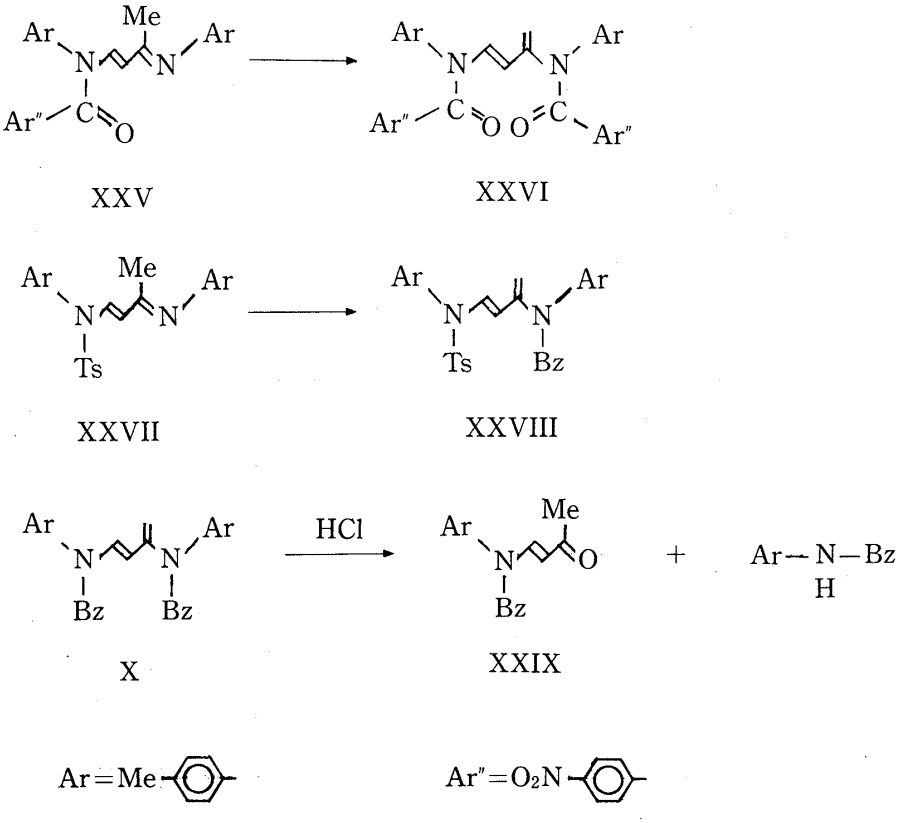


Chart 6

of the *N*-acyl-*p*-toluidino group at the 3-position of VIII is resistant to base-catalyzed alcoholysis.

Hydrochloric acid-catalyzed hydrolysis of X was also examined. The ^{1}H-NMR spectrum of X in dioxane-d_8 showed signals at δ 4.80 (4-position, singlet), 5.02 (4-position, singlet), 5.28 (2-position, doublet, J=14 Hz) and 7.92 (1-position, doublet, J=14 Hz). At 38 min after the addition of a solution of sulfuric acid-d_2 in deuterium oxide (a small amount of methanol-d_4 was added to the mixture to ensure dissolution),signals due to X had disappeared and signls of 4-(*N*-benzoyl-*p*-toluidino)-3-buten-2-one (XXIX) were observed at δ 5.25 (3-position, doublet, J=14 Hz) and 8.62 (4-position, doublet, J=14 Hz) and a multiplet signal of the 2- and 6-positions of *N*-benzoyl-*p*-toluidine was observed at δ 8.00. Compound XXIX and *N*-benzoyl-*p*-toluidine were obtained when a solution of X in aqueous dioxane containing hydrochloric acid was allowed to stand for 120 min at room temperature.

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 abbreviations are used: singlet (s), doublet (d) and double quartet (dq).

Compound XX was prepared according to the previous paper.[1] Compounds I, II, V, IX, X, XI and XXIX were prepared according to an earlier paper.[2] Compound IV[6,8] and compound III[6,7] were prepared according to the cited references.

The samples of III, XI, XXIX, BzOH, *p*-chlorobenzoic acid, *p*-nitrobenzoic acid, *N*-benzoyl-*p*-toluidine, *N*-(*p*-chlorobenzoyl)-*p*-toluidine, *N*-(*p*-nitrobenzoyl)-*p*-toluidine, *N*-tosyl-*p*-toluidine and methyl *p*-nitrobenzoate described in this section were identical with the authentic samples on the basis of mixed melting point measurement and comparison of their IR spectra.

1-(*N*-Acetyl-*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (XII), 1,3-Bis(*N*-acetyl-*p*-toluidino)-1,3-butadiene (XIII) and 1-(*N*-Acetyl-*p*-toluidino)-3-(*N*-benzoyl-*p*-toluidino)-1,3-butadiene (XIV) ——A solution of 0.78 g of AcCl in 10 ml of anhydrous benzene was added portionwise to a cold solution of 1.32 g of XI and 2 g of Et_3N in 30 ml of anhydrous benzene. The mixture was allowed to stand for one day at room temperature, and was then washed successively with 7% $NaHCO_3$ and H_2O, and dried over K_2CO_3. The mixture was concentrated under reduced pressure and the residue was treated with petroleum ether under ice cooling. The precipitate (0.51 g) was collected and recrystallized from petroleum benzine to give 0.34 g of XIII. mp 126°C. *Anal.* Calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 76.67; H, 7.04; N, 7.93. ^{1}H-NMR ($CDCl_3$) δ: 1.87 (3H, CH_3 of acetyl, s), 2.15 (3H, CH_3 of acetyl, s) 2.33 (3H, CH_3, s), 2.43 (3H, CH_3, s), 5.07 (1H, 4-position, s), 5.10 (1H, 4-position, s), 5.05 (1H, 2-position, d, J=15 Hz) and 7.95 (1H, 1-position, d, J=15 Hz). The mother liquor was concentrated to give 0.99 g of crude XII. XII (3.06 g) was dissolved in 50 ml of anhydrous benzene, and 1.05 g of Et_3N was added to the solution. A solu tion of 1.54 g of BzCl in 5 ml anhydrous benzene was then added with stirring. The mixture was allowed to stand for 2 h at room temperature, washed successively with 7% $NaHCO_3$ and H_2O, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was recrystallized from petroleum benzine to give 1.35 g of XIV. mp 168°C. *Anal.* Calcd for $C_{27}H_{26}N_2O_2$: C, 79.35; H, 6.29; N, 6.95. Found: C, 79.00; H, 6.38; N, 6.82. ^{1}H-NMR ($CDCl_3$) δ: 1.87 (3H, CH_3 of acetyl, s), 2.30 (3H, CH_3, s), 2.42 (3H, CH_3, s), 4.85 (1H, 4-position, s), 5.02 (1H, 4-position, s), 5.02 (1H, 2-position, d, J=14 Hz) and 8.07 (1H, 1-position, d, J=14 Hz).

1-(*N*-Benzoyl-*p*-toluidino)-3-(*N*-tosyl-*p*-toluidino)-1,3-butadiene (XVII)——*p*-Toluenesulfonyl chloride (2.72 g) was added to a solution of 3.68 g of IX and 2 g of Et_3N in 8 ml of CH_2Cl_2 and the mixture was allowed to stand for one day at room temperature. The mixture 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 benzene to give 3.87 g of XVII. mp 126°C. *Anal.* Calcd for $C_{32}H_{30}N_2O_3S \cdot 1/2C_6H_6$: C, 74.84; H, 5.92; N, 4.99. Found: C, 74.85; H, 5.93; N, 4.73. ^{1}H-NMR ($CDCl_3$) δ: 2.35 and 2.40 (9H, $3CH_3$), 4.93 (1H, 4-position, s), 5.03 (1H, 4-position, s), 5.18 (1H, 2-position, d, J=14 Hz) and 7.95 (1H, 1-position, d, J=14 Hz).

1-*N*-(*p*-Chlorobenzoyl)-*p*-methylphenylamino-3-(*p*-methylphenylimino)-1-butene (XXI)——A solution of 6.30 g of *p*-chlorobenzoyl chloride in 50 ml of CH_2Cl_2 was added to a solution of 10.47 g of the hydrochloride of XI and 7 g of Et_3N in 150 ml of CH_2Cl_2 under cooling. The mixture was allowed to stand for 30 min at room temperature, washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from CH_2Cl_2–petroleum ether to give 12.18 g of XXI. mp 156°C. *Anal.* Calcd for $C_{25}H_{23}N_2OCl$: C, 74.52; H, 5.75; N, 6.95. Found: C, 74.28; H, 5.78; N, 6.78. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (3H, 4-position, s), near 2.32 (6H, $2CH_3$), 5.63 (2-position, d, J=15 Hz) and 8.30 (1-position, d, J=15 Hz). Besides these signals, weak signals of the conformational isomer were observed at δ 5.27 (2-position, d, J=15 Hz) and 8.17 (1-position, d, J=15 Hz).

1,3-Bis[*N*-(*p*-chlorobenzoyl)-*p*-toluidino]-1,3-butadiene (XXII)——*p*-Chlorobenzoyl chloride (3.94 g) was added to a solution of 6.05 g of XXI and 2 g of Et_3N in 10 ml of CH_2Cl_2. The mixture was allowed to stand for 3 h at room temperature, washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3 and concentrated under reduced pressure. The residue was collected and washed with ether to give 6.03 g of XXII. mp 152°C. *Anal.* Calcd for $C_{32}H_{26}Cl_2N_2O_2$: C, 70.32; H, 4.95; N, 5.29. Found: C, 70.88; H, 4.69; N, 5.03. ^{1}H-NMR ($CDCl_3$) δ: 2.32 (3H, CH_3, s), 2.35 (3H, CH_3, s), 4.88 (1H, 4 position, s), 5.08 (1H, 4-position, s), 5.38 (1H, 2-position, d, $J=14$ Hz) and 7.85 (1H, 1-position, d, $J=14$ Hz).

1-[*N*-(*p*-Nitrobenzoyl)-*p*-methylphenylamino]-3-(*p*-methylphenylimino)-1-butene (XXV)——A solution of 2.05 g of *p*-nitrobenzoyl chloride in 20 ml of CH_2Cl_2 was added to a solution of 3.49 g of the hydrochloride of XI and 3 g of Et_3N in 40 ml of CH_2Cl_2 under cooling. The mixture was allowed to stand for 80 min at room temperature, washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. The residue was recrystallized from CH_2Cl_2–petroleum benzine to give 3.80 g of XXV. mp 155°C. *Anal.* Calcd for $C_{25}H_{23}N_3O_3$: C, 72.62; H, 5.61; N, 10.16. Found: C, 72.48; H, 5.61; N, 10.03. ^{1}H-NMR ($CDCl_3$) δ: 2.03 (3H, 4-position, s), near 2.30 (6H, $2CH_3$), 5.67 (1H, 2-position, d, $J=15$ Hz) and 8.30 (1H, 1-position, d, $J=15$ Hz).

1,3-Bis[*N*-(*p*-nitrobenzoyl)-*p*-toluidino]-1,3-butadiene (XXVI)——*p*-Nitrobenzoyl chloride (2.23 g) was added to a solution of 4.13 g of XXV and 1.3 g of Et_3N in 20 ml of CH_2Cl_2. The mixture was allowed to stand for one day at room temperature, washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. The residue was collected and washed with ether to give 4.83 g of XXVI. mp>230°C. *Anal.* Calcd for $C_{32}H_{26}N_4O_6$: C, 68.32; H, 4.66; N, 9.96. Found: C, 68.14; H, 4.58; N, 9.88. ^{1}H-NMR ($CDCl_3$) δ: 2.37 (6H, $2CH_3$, s), 5.02 (1H, 4-position, s), 5.20 (1H, 4-position, s) and 5.45 (1H, 2-position, d, $J=15$ Hz).

1-(*N*-Tosyl-*p*-toluidino)-3-(*N*-benzoyl-*p*-toluidino)-1,3-butadiene (XXVIII)——A solution of 0.79 g of BzCl in 3 ml of benzene was added to a solution of 1.82 g of XXVII and 0.8 g of Et_3N in 20 ml of benzene. The mixture was allowed to stand for one day at room temperature, washed successively with 7% $NaHCO_3$ and H_2O, dried over K_2CO_3, and concentrated under reduced pressure. The residue (1.90 g) was recrystallized from EtOH to give 1.60 g of XXVIII. mp 172°C. *Anal.* Calcd for $C_{32}H_{30}N_2O_3S$: C, 73.54; H, 5.78; N, 5.36. Found: C, 73.69; H, 5.67; N, 4.96. ^{1}H-NMR ($CDCl_3$) δ: 2.35 and 2.40 (9H, $3CH_3$), 4.80 (1H, 4-position, s), 4.95 (1H, 4-position, s), 4.93 (1H, 2-position, d, $J=14$ Hz) and 7.63 (1H, 1-position, d, $J=14$ Hz).

Hydrolysis of X——A mixture of 0.35 g of 46% NaOH, 1 ml of H_2O and 3 ml of MeOH was added to a solution of 0.94 g of X in 5 ml of THF. The mixture was warmed at 40°C for 20 min, then 15 ml of 7% $NaHCO_3$ was added and the whole was concentrated under reduced pressure. The residue was extracted with ether. The ether solution was extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was treated as usual to give 0.23 g of BzOH. The ether layer was concentrated, and the residue (its ^{1}H-NMR spectrum showed a singlet signal at δ 3.78 in $CDCl_3$, suggesting that methyl benzoate was contained in the mixture) was fractionated by column chromatography on Al_2O_3 with benzene and MeOH. From the first fraction (eluted with benzene), 0.12 g of XI was obtained by recrystallization from 70% EtOH. From the second fraction (eluted with benzene–MeOH), 0.25 g of XV was obtained. It was dissolved in 2 ml of THF, and the solution was added to 14 ml of 0.05 N HCl with stirring, then 15 ml of ether was added. The mixture was stirred for 20 min at room temperature. The ether layer was washed with 0.05 N HCl and extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was treated as usual to give 15 mg of BzOH. The ether layer was concentrated, and the ^{1}H-NMR spectrum ($CDCl_3$) of the residue showed a pattern attributable to XVI.

Alkaline Hydrolysis of XVII——A solution of 0.32 g of NaOH in 4.7 g of H_2O was added to a warm solution of 2.09 g of XVII in 10 ml of THF, and 8 ml of MeOH was added to the mixture to ensure dissolution. The mixture was warmed at 40°C for 20 min, and 20 ml of 7% $NaHCO_3$ was added. The whole was concentrated under reduced pressure, and the residue was extracted with ether. The ether solution was extracted with 1 N NaOH. The $NaHCO_3$ layer was treated as usual to give 0.34 g of BzOH. The NaOH layer was treated as usual to give a small amount of *N*-tosyl-*p*-toluidine. The ether layer was concentrated to give 1.55 g of crude XVIII which could not be crystallized. ^{1}H-NMR ($CDCl_3$) δ: 6.30 (2-position, dq, $J=1$, 9 Hz) and 8.30 (1-position, d, $J=9$ Hz). Besides these signals, weak signals of the conformational isomer were observed at δ 6.43 (2-position, dq, $J=1$, 9 Hz) and 8.40 (1-position, d, $J=9$ Hz). A solution of 1.55 g of XVIII in anhydrous ether was saturated with dry HCl and the precipitate was collected and recrystallized from MeOH to give 1.06 g of the hydrochloride of XVIII. mp 153°C. *Anal.* Calcd for $C_{25}H_{26}N_2O_2S\cdot HCl$: C, 65.99; H, 5.98; N, 6.16. Found: C, 65.45; H, 5.95; N, 5.83. ^{1}H-NMR (CD_3OD) δ: 6.53 (2-position, d, $J=11$ Hz) and 8.97 (1-position, d, $J=11$ Hz). Besides these signals, weak signals of the conformational isomer were observed at δ 6.43 (2-position, d, $J=11$ Hz) and 9.07 (1-position, d, $J=11$ Hz).

HCl-Catalyzed Hydrolysis of XVIII——A warm solution of 0.91 g of the hydrochloride of XVIII in 10 ml of MeOH was added to 60 ml of 0.1 N HCl with stirring, then 30 ml of ether was added. The mixture was stirred for 50 min at room temperature. The ether layer was washed with 0.1 N HCl and extracted successively with 7% $NaHCO_3$ and 1 N NaOH. No organic substance could be detected in the $NaHCO_3$ layer. The NaOH layer was treated as usual to give 30 mg of *N*-tosyl-*p*-toluidine. The ether layer was concentrated and the residue was recrystallized from petroleum benzine to give 0.47 g of XIX. mp 119°C. *Anal.* Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.56; H, 5.70; N, 4.00. ^{1}H-NMR ($CDCl_3$) δ: 2.28

(3H, CH_3, s), 2.40 (3H, CH_3, s), 2.45 (3H, CH_3, s), 5.82 (1H, α-position, dq, $J=1$, 8 Hz) and 9.80 (1H, aldehyde, d, $J=8$ Hz). ^{1}H-NMR (CD_3OD) δ: 2.22 (3H, CH_3, s), 2.38 (3H, CH_3, s), 2.43 (3H, CH_3, s), 5.87 (1H, α-position, dq, $J=1$, 8 Hz) and 9.72 (1H, aldehyde, d, $J=8$ Hz).

Reaction of XX and *p*-Toluidine in the Presence of *n*-Butyllithium——A 15% solution of *n*-butyllithium in *n*-hexane (0.46 ml) was added to a solution of 0.12 g of *p*-toluidine in 1 ml of anhydrous THF under an N_2 atmosphere, and a solution of 0.31 g of XX in 3 ml of anhydrous THF was added. The mixture was allowed to stand for 3 d at room temperature, then 3 ml of 7% $NaHCO_3$ was added. The whole was concentrated under reduced pressure, and the residue was extracted with ether. The ether solution was extracted with 1 N NaOH. No organic substance could be detected in the $NaHCO_3$ layer. The NaOH layer was treated as usual to give 80 mg of *N*-tosyl-*p*-toluidine. The ether layer was concentrated and the residue was fractionated by preparative thin-layer chromatography on silica gel with a mixture of benzene–AcOEt (4: 1) as a developing solvent to give 10 mg of XI and a small amount of III.

Alkaline Hydrolysis of XXII——One ml of H_2O and 0.9 ml of 1 N NaOH were added to a warm solution of 0.40 g of XXII in 3 ml of THF, and 3 ml of MeOH was added to the mixture to ensure dissolution. The whole was warmed at 40°C for 10 min, then 10 ml of 7% $NaHCO_3$ was added. The mixture was concentrated under reduced pressure, and the residue was extracted with ether. The $NaHCO_3$ layer was treated as usual to give 85 mg of *p*-chlorobenzoic acid. The ether layer was concentrated. The ^{1}H-NMR spectrum of the residue showed a pattern attributable to a mixture of XXIII and methyl *p*-chlorobenzoate. The residue was fractionated by column chromatography on Al_2O_3 with benzene and MeOH. From the first fraction (eluted with benzene), a small amount of *N*-(*p*-chlorobenzoyl)-*p*-toluidine was obtained. From the second fraction (eluted with MeOH), 0.2 g of XXIII was obtained.

Preparation of V by Hydrolysis of XXII——A mixture of 8.5 ml of 1.18 N tetramethylammonium hydroxide and 33 ml of H_2O was added to a solution of 2.65 g of XXII in 100 ml of acetone. The mixture was warmed at 40°C for 2 h, then 20 ml of 7% $NaHCO_3$ was added. The whole was concentrated under reduced pressure, and the residue was extracted with ether. The $NaHCO_3$ layer was treated as usual to give 0.37 g of *p*-chlorobenzoic acid. The ether layer was concentrated, and the residue (2.75 g) was dissolved in 5 ml of THF. The solution was added to 280 ml of 0.05 N HCl with stirring, and 100 ml of ether was further added. The mixture was stirred for 20 min at room temperature. The ether layer was washed with 0.1 N HCl and extracted with 7% $NaHCO_3$. The $NaHCO_3$ layer was treated as usual to give 0.1 g of *p*-chlorobenzoic acid. The ether layer was concentrated. The residue (0.94 g, XXIV) was dissolved in 20 ml of MeOH, and 3 ml of 1 N NaOH and 2 ml of H_2O were added to the solution. The mixture was allowed to stand overnight at room temperature, and 10 ml of 7% $NaHCO_3$ was added. The whole was concentrated under reduced pressure and the residue was extracted with ether. The $NaHCO_3$ layer was treated as usual to give 0.23 g of *p*-chlorobenzoic acid. The ether layer was concentrated and the residue was subjected to column chromatography on Al_2O_3 with benzene to give 0.17 g of V.

Alkaline Hydrolysis of XXI——One ml of 1 N NaOH was added to a warm solution of 0.4 g of XXI in 4 ml of EtOH. The mixture was stirred for 2.5 h at room temperature. The precipitated XI (0.23 g) was collected. Ten ml of 7% $NaHCO_3$ was added to the filtrate, the mixture was concentrated under reduced pressure, and the residue was extracted with ether. The $NaHCO_3$ layer was treated as usual to give 0.1 g of *p*-chlorobenzoic acid. The ether layer was concentrated and the residue was subjected to preparative thin-layer chromatography on silica gel with a mixture of benzene–AcOEt (4: 1) as a developing solvent to give a small amount of *N*-(*p*-chlorobenzoyl)-*p*-toluidine. The ^{1}H-NMR spectrum ($CDCl_3$) of the upper layer showed a pattern identical with that of ethyl *p*-chlorobenzoate.

MeONa-Catalyzed Alcoholysis of XXI——A solution of MeONa in MeOH (prepared from 0.05 g of Na and 5 ml of MeOH) was added to a solution of 1.03 g of XXI in a mixture of 12 ml of THF and 10 ml of MeOH. The mixture was allowed to stand for 6 min at room temperature, then saturated with CO_2. The mixture was concentrated under reduced pressure, and the residue was extracted with ether. The ether solution was extracted with 0.1 N HCl. The HCl layer was treated as usual to give 0.42 g of XI. The ether layer was concentrated, and the residue was distilled under reduced pressure to give 0.24 g of methyl *p*-chlorobenzoate It was shown to be identical with an authentic sample by comparison of their IR spectra

Alkaline Hydrolysis of XXV——One ml of 1 N NaOH and 7 ml of H_2O were added to a warm solution of 0.41 g of XXV in 8 ml of EtOH, and the mixture was stirred for 1 h at room temperature. The precipitate (XI, 0.18 g) was collected. Twenty ml of 7% $NaHCO_3$ was added to the filtrate, and the mixture was concentrated under reduced pressure. The residue was extracted with ether. The $NaHCO_3$ layer was treated as usual to give 0.14 g of *p*-nitrobenzoic acid. The ether layer was concentrated, and the residue was subjected to preparative thin-layer chromatography on silica gel with a mixture of benzene–AcOEt (4: 1) as a developing solvent to give 5 mg of *N*-(*p*-nitrobenzoyl)-*p*-toluidine.

MeONa-Catalyzed Alcoholysis of XXV——A solution of MeONa in MeOH (prepared from 0.055 g of Na and 5 ml of MeOH) was added to a solution of 1.03 g of XXV in a mixture of 12 ml of THF and 10 ml of MeOH. The whole was allowed to stand for 6 min at room temperature, and was then saturated with CO_2. The mixture was concentrated under reduced pressure, and the residue was extracted with ether. The ether solution was extracted with 0.1 N HCl. The HCl layer was treated as usual to give 0.32 g of XI. The ether layer was treated as usual to give 0.24 g of methyl *p*-nitrobenzoate.

MeONa-Catalyzed Hydrolysis of XXII——A solution of MeONa in MeOH (prepared from 0.12 g of Na and 6 ml of MeOH) was added to a solution of 2.87 g of XXII in a mixture of 17 ml of THF and 20 ml of MeOH. The whole was allowed to stand for 6 min at room temperature, and was then saturated with CO_2. The mixture was concentrated under reduced pressure, and the residue was extracted with ether. The ether solution was concentrated and the residue was fractionated by column chromatography on Al_2O_3 with benzene and EtOH to give 0.67 g of methyl *p*-chlorobenzoate, 0.14 g of *N*-(*p*-chlorobenzoyl)-*p*-toluidine and 1.44 g of XXIII.

MeONa-Catalyzed Alcoholysis of I——A solution of MeONa in MeOH (prepared from 0.07 g of Na and 3 ml of MeOH) was added to a solution of 1.10 g of I in a mixture of 10 ml of THF and 10 ml of MeOH. The whole was allowed to stand for 6 min at room temperature, and was then saturated with CO_2. The mixture was concentrated under reduced pressure, and the residue was extracted with ether. The ether solution was extracted with 30 ml of 0.1 N HCl. The HCl layer was treated as usual to give 0.60 g of XI. The ether layer was concentrated and the residue was distilled under reduced pressure to give 0.27 g of methyl benzoate. It was shown to be identical with an authentic sample by comparison of their IR spectra.

HCl-Catalyzed Hydrolysis of X——Five ml of 1 N HCl was added to a solution of 2.36 g of X in 25 ml of dioxane. The mixture was allowed to stand for 2 h at room temperature. Ten ml of 7% $NaHCO_3$ was added, and the whole was concentrated under reduced pressure. The residue was extracted with benzene. The benzene solution was concentrated under reduced pressure, and the residue was subjected to preparative thin-layer chromatography on silica gel with a mixture of benzene–AcOEt (4: 1) as a developing solvent to give 0.45 g of *N*-benzoyl-*p*-toluidine and 0.14 g of XXIX.

References and Notes

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