# PREPARATION OF 3-SUBSTITUTED QUINOLINES. II. PREPARATION AND CYCLODEHYDRATION OF α-ALKYL- AND α-PHENYL-β-ARYLAMINOACROLEIN DERIVATIVES

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Abstract —— α-Methyl-β-arylaminoacroleins were prepared by the hydrolysis of 2-methyl-1-arylamino-3-arylimino-1-propene derivatives. α-Ethyl- and α-phenyl-β-arylaminoacroleins were prepared by the reaction of arylamines and 2-substituted 1,1,3,3-tetraethoxypropane derivatives. 3-Methyl-, 3-ethyl- and 3-phenylquinolines were obtained from α-methyl-, α-ethyl and α-phenyl-β-arylaminoacroleins on heating with aluminum bromide in good yields.
α-Bromo-β-anilinoacrolein (**9b**) was prepared by the reaction of β-anilinoacrolein (**6b**) and *N*-bromosuccinimide. Reaction of **9b** and aluminum bromide did not afford 3-bromoquinoline.

In a previous paper[1] we reported preparation of 3-benzylquinolines by the cyclodehydration of α-benzyl-β-arylaminoacrolein derivatives with aluminum halides (Combes reaction).
In this paper we wish to report the preparation and cyclodehydration of α-alkyl- and α-phenyl-β-arylaminoacrolein derivatives.
2-Methyl-1-phenylamino-3-phenylimino-1-propene (**1b**) was prepared by addition of two equivalent amount of aniline hydrochloride to a solution of 1,1,3,3-tetraethoxy-2-methylpropane (**2b**) in 85 % aqueous ethanol followed by neutralization of the deposited hydrochloride of **1b** (Chart 1). α-Methyl-β-anilinoacrolein (**3b**) was obtained in a good yield by hydrolysis of **1b** in the same manner that employed for the hydrolysis of 1-arylamino-3-arylimino-1-propene to give β-arylaminoacrolein,[2]

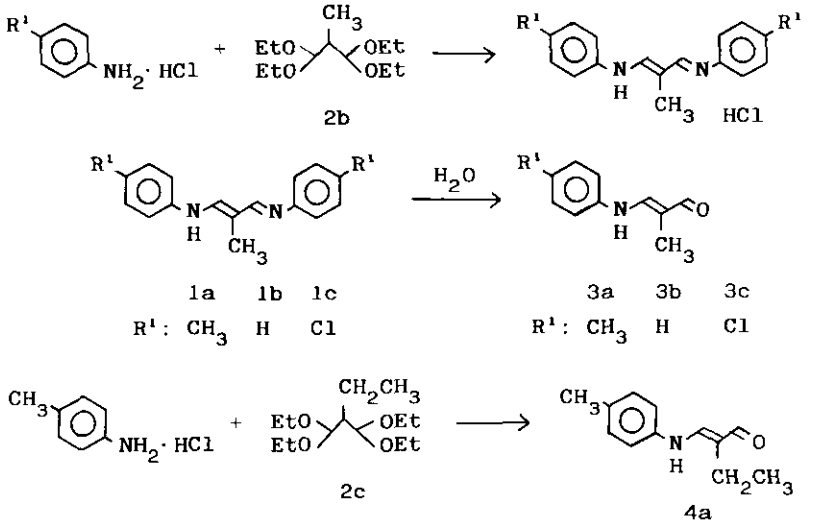


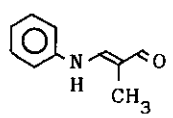
Chart 1

*i*.e., the substrate was heated in aqueous ethanolic solution in the presence of acetic acid and sodium acetate. α-Methyl-β-(*p*-toluidino)acrolein (**3a**) and α-methyl-β-(*p*-chloroanilino)acrolein (**3c**) were prepared by the same method (Chart 1).

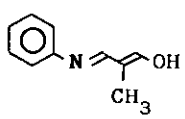
α-Ethyl-β-(*p*-toluidino)acrolein (**4a**) was obtained directly on standing a solution of equimolar amounts of 1,1,3,3-tetraethoxy-2-ethylpropane (**2c**) and *p*-toluidine hydrochloride in 86 % aqueous ethanol for 50 min at room temperature (Chart 1).

Pino[3] obtained **3b** by heating of hydrobromide of **1b** with water which was prepared by the reaction of aniline and β-bromomethacrylaldehyde. The melting point described by Pino for **3b** is identical with that of our sample. He proposed the structure of 2-phenyliminomethyl-1-propenol (**3b-I**) for **3b** on the basis of violet color reaction with ferric chloride (Chart 2).

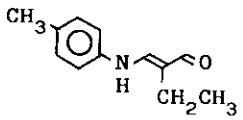
The compound **4a** as well as **3b** gave intense violet solution on addition of ferric chloride. According to Pino's opinion, the structure of **4a** should be 2-(*p*-methylphenyliminomethyl)-1-butenol (**4a-I**) (Chart 2). The structure of **4a** was proved to be not **4a-I** but **4a** by the following experiment. The $^1$H nmr spectrum (chloroform-*d*) of **4a** showed that **4a** exists as a mixture of two conformational isomers in a ratio of 3:1 (Table 1). The minor conformer was concluded to be a s-*cis* form (**4a-II**) on the basis of the long range coupling ($J$ = 4 Hz) between the protons of aldehyde and β-position corresponds to the 'W' configuration of the bond. The major conformer



**3b**

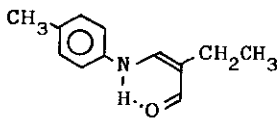


**3b-I**



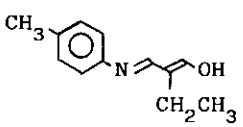
**4a**

(s-*trans* form)

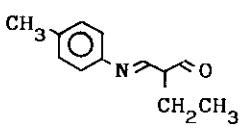


**4a-II**

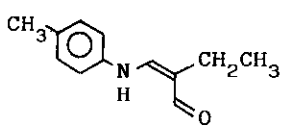
(s-*cis* form)



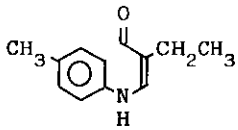
**4a-I**



**4a-V**



**4a-III**



**4a-IV**

Chart 2

Table 1. $^{13}C$ and $^{1}H$ nmr Data of **4a**

| position | $^{13}C$ (δ) ($CD_3SOCD_3$) | $^{1}H$ (δ) ($CD_3SOCD_3$) | $^{1}H$ (δ) ($CDCl_3$, s-*trans* form) | $^{1}H$ (δ) ($CDCl_3$, s-*cis* form) |
|---|---|---|---|---|
| CHO | 188.62 (d) | 9.10 (s) | 9.15 (s) | 9.32 (d, $J$=4 Hz) |
| α | 118.64 (s) | | | |
| β | 147.88 (d) | 7.62[a] (d, $J$=13 Hz) | 7.30[a] (d, $J$=13 Hz) | 7.22[b] (dd, $J$=4 and 12 Hz) |
| 1 | 138.35 (s) | | | |
| 2,6 | 115.27 (d) | 7.20 (d, $J$=8.5 Hz) | 7.15 or 6.96 (d, $J$=9 Hz) | 7.11 or 6.92 (d, $J$=9 Hz) |
| 3,5 | 129.08 (d) | 7.12 (d, $J$=8.5 Hz) | 6.96 or 7.15 (d, $J$=9 Hz) | 6.92 or 7.11 (d, $J$=9 Hz) |
| 4 | 130.41 (s) | | | |
| $CH_3$ | 20.08 (q) | 2.25 (s) | observed as a multiplet signal at near δ 2.32 | |
| $\underline{CH_2}$-$CH_3$ | 14.61 (t) | 2.29 (q, $J$=7 Hz) | | |
| $CH_2$-$\underline{CH_3}$ | 12.80 (q) | 0.93 (t, $J$=7 Hz) | 1.06 (t, $J$=8 Hz) | 1.13 (t, $J$=8 Hz) |
| NH | | 9.18[c] (d, $J$=13 Hz) | 7.08[c] (d, $J$=13 Hz) | 11.56[c] (d, $J$=12 Hz) |

[a] changed into a singlet signal on addition of $D_2O$.

[b] changed into a doublet signal ($J$=4 Hz) on addition of $D_2O$.

[c] disappeared on addition of $D_2O$.

was proved to be a s-*trans* form (**4a**) by the following experiments (Chart 2). The $^{1}H$ nmr spectrum of **4a** (dmso-$d_6$) showed similar pattern to that of the major conformer in chloroform-*d* solution (Table 1). The $^{13}C$ signal at δ 20.08 (dmso-$d_6$, triple quartet, $J_q$ = 62 Hz, $J_t$ = 2 Hz under non-decoupling condition) changed into a quartet signal ($J$ = 62 Hz) on irradiation of the protons at δ 7.12 with low power. The $^{13}C$ signal at δ 115.27 (double double doublet, $J$ = 160, 5 and 3 Hz) changed into a singlet signal on irradiation of the protons at δ 7.20 with high power. Irradiation (pulse delay time) of NH proton at δ 9.18 (3.6 % dmso-$d_6$ solution, under nitrogen atmosphere) caused 6 % nuclear Overhauser effect (NOE) on the signal at δ 7.20 and 5 % NOE on the signal at δ 2.29 (methylene group), and not on the signals at δ 7.12 and at δ 9.10 (aldehyde). These expriments confirmed the assignments of $^{13}C$ as well as $^{1}H$ signals of 3,5- and 2,6-positions of aromatic ring. The $^{13}C$ signal at δ 115.27 changed into a double doublet signal ($J$ = 160 and 5 Hz) on irradiation of NH proton at δ 9.18 with low power. It means that the carbon atoms of 2,6-positions combine with the hydrogen atom at δ 9.18 (NH) through three or four bonds. This can not be explained with the structure **4a**-I and possible another conformer of **4a** (**4a**-III) was also ruled out by these experiments (Chart 2). Furthermore, irradiation (pulse delay time) of the protons at δ 7.20 caused 5 % NOE on the signal at δ 9.18 (NH), 10 % NOE on the signal at δ 7.62 (β-position) and 5 % NOE on the signal at δ 7.12 (3,5-positions). These observations support the structure **4a**, and ruled out another conformer **4a**-IV (Chart 2). Another possible structure **4a**-V was ruled out from the coupling pattern of the signal at δ 2.29 (methylene group) in the $^{1}H$ nmr spectrum (Chart 2).

As stated in the earlier part of this report, **4a** was obtained by the reaction of **2c** and *p*-toluidine hydrochloride in contrast to the reaction of 1,1,3,3-tetraethoxypropane (**2a**) and *p*-toluidine hydrochloride which gave 1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (**5a**)[2,4] and β-(*p*-toluidino)acrolein (**6a**) could not be detected in the reaction mixture. The reaction of *p*-toluidine hydrochloride with **6a** as well as with **4a** was followed by the $^{1}H$ nmr spectrum of the reaction solution. The spectrum of a methanol-$d_4$ solution of **6a** showed weak signals of **5a** hydrochloride at δ 8.55 (d, $J$ = 12 Hz, 1,3-positions) and 6.17 (t, $J$ = 12 Hz, 2-position) at 2 min after addition of a solution of an equimolar amount of *p*-toluidine hydrochloride in deuterium oxide. Relative integrated intensity of each signal showed that **6a** and **5a** hydrochloride exist in a ratio of 1:1 at 14 min after

addition. After 100 min, the spectrum showed only the signal of **5a** hydrochloride. The $^1$H nmr spectrum of a methanol-$d_4$ solution of **4a** did not show detectable change at 5 min after addition of a solution of an equimolar amount of *p*-toluidine hydrochloride in deuterium oxide. After 140 min, the spectrum showed signals of 2-ethyl-1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (**7a**) hydrochloride at δ 8.47 (s, 1,3-positions) and 2.72 (q, $J$ = 8 Hz, methylene group), and relative integrated intensity of each signal showed that **4a** and hydrochloride of **7a** exist in a ratio of 1:1. After 480 min, the spectrum still showed weak signals of **4a**.

α-Ethyl-β-anilinoacrolein (**4b**), α-ethyl-β-(*p*-chloroanilino)acrolein (**4c**), α-phenyl-β-(*p*-toluidino)acrolein (**8a**), α-phenyl-β-anilinoacrolein (**8b**) and α-phenyl-β-(*p*-chloroanilino)acrolein (**8c**) were prepared in the same manner as the preparation of **4a** (Chart 3).

As a preliminary experiment for the cyclodehydration of α-substituted β-arylaminoacroleins, **4c** was heated at 90-100°C with three equivalent amount of aluminum bromide for 30 min to give 3-ethyl-6-chloroquinoline in 50 % yield together with 23 % of **4c**. 3-Methylquinoline, 3-ethylquinoline and 3-phenylquinoline were heated respectively with three equivalent amount of aluminum bromide at 120°C for 5 h to recover 87, 96 and 72 % of the starting materials.

3-Substituted quinolines were obtained in good yields on heating α-substituted β-arylaminoacroleins with three equivalent amount of aluminum bromide at 120°C for 5 h (Chart 3). 3-Phenyl-6-chloroquinoline could not be obtained on heating **8c** with aluminum bromide. It was prepared by heating **8c** with three equivalent amount of aluminum chloride in 28 % yield.

Reliquet, et al.[5] briefly reported that α-bromo-β-anilinoacrolein (**9b**) and α-bromo-β-(*p*-toluidino)acrolein (**9a**) were obtained from **5b** and **5a** by the reaction with *N*-bromosuccinimide (NBS). We obtained 2-bromo-1-phenylamino-3-phenylimino-1-propene (**10b**) and 2-bromo-1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (**10a**) by bromination of **5b** and of **5a** with NBS. Hydrolysis of **10b** and **10a** in the same manner as preparation of **3b** gave **9b** as well as **9a** in good yields (Chart 4). The compounds **9b** and **9a** were also obtained by bromination of β-anilinoacrolein (**6b**) and of β-(*p*-toluidino)acrolein (**6a**) with NBS (Chart 4).

α-Bromo-β-(2,4-dibromoanilino)acrolein (**11**) and a small amount of quinoline were obtained when **9b** was heated at 80°C with three equivalent amount of aluminum

bromide for 30 min. The former was identical with authentic sample prepared by bromination of β-(2,4-dibromoanilino)acrolein (**12**) with NBS (Chart 4). Among the above mentioned materials, a small amount of a liquid was obtained on preparative thin layer chromatography (PTLC) of the reaction mixture. It's $^1$H nmr spectrum (benzene-$d_6$) was identical with that of 5,8-dibromoquinoline (Chart 4). Quinoline, 5,8-dibromoquinoline and 8-bromoquinoline were obtained from the reaction mixture in which **9b** was heated at 120°C with three equivalent amount of aluminum bromide for 5 h. 3-Bromoquinoline could not be detected in the reaction mixture (Chart 4). It is clear that debromination at α-position of **9b** and bromination on aromatic ring occured during the reaction. Reaction of **9b** with aluminum chloride caused polymerization, and no quinolines were detected in the reaction mixture.

Quinoline (91 %) was recovered on heating at 120°C with three equivalent amount of aluminum bromide for 5 h, and 29 % of quinoline and 11 % of aniline were obtained by heating **6b** under the same conditions. Brominating agents were not contained in aluminum bromide used. When 3-bromoquinoline was heated at 120°C with three equivalent amount of aluminum bromide for 5 h, 73 % of starting material was recovered and a small amount of 3,5-dibromoquinoline was detected in the reaction mixture (Chart 4). Debromination and bromination might occur during the reaction.

Eisch[6] reported that the heating of 3-bromoquinoline hydrochloride at 300°C caused debromination as evidenced by the isolation of quinoline from the product and by the detection of free bromine in the reaction mixture. He reported the formation of 4-bromo- and 5-bromoquinoline and polybromoquinolines at prolonged heating in the same reaction. It is known that 5,8-dibromoquinoline formed on the reaction of quinoline and bromine in the presence of aluminum bromide.[7] Mare, et al.[8] reported that chemical behavior of 3-bromoquinoline in bromination is similar to that of quinoline. Altschul and Bartlett[9] evaluated the equilibrium constants of debromination of α-bromoketones. They suggested the formation of positive bromine. Griesbaum and Kibar[10] reported the debromination of α-bromoketone on heating with quinoline and other bases. They proved the hydrogen acted as a reducing agent to be derived from both the starting bromoketone and bases used.

Presumably debromination occured as the first step in the reaction of **9b** and aluminum bromide, and **6b** formed was converted into quinoline by cyclodehydration, the latter was brominated by positive bromine in the presence of aluminum bromide. Aluminium bromide is, therefore, not suitable as a cyclodehydrating agent for the

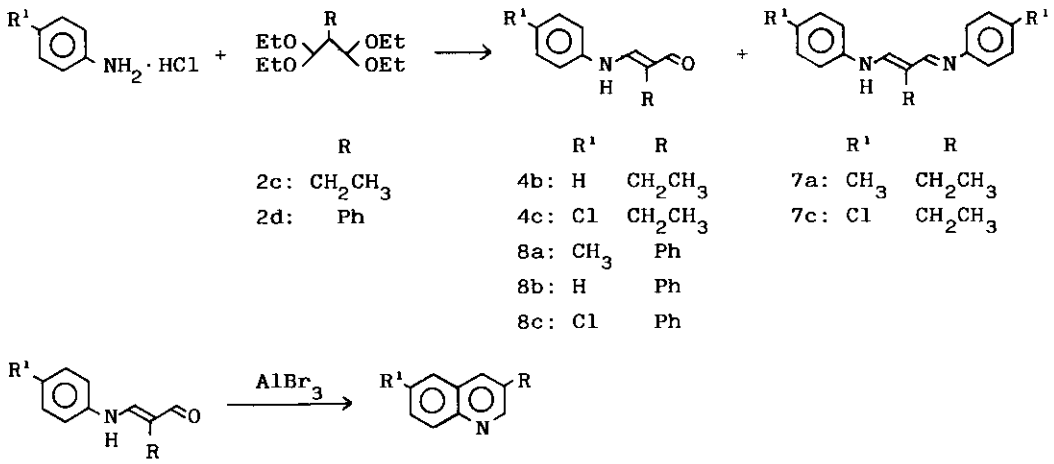



Chart 3

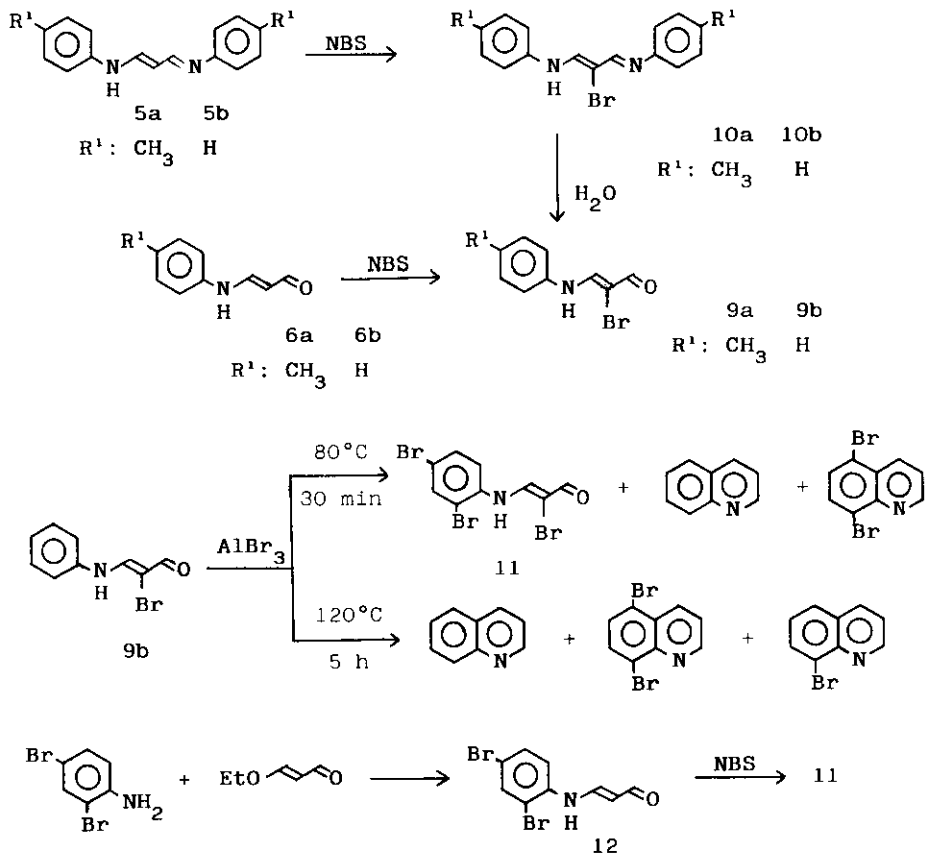



Chart 4

preparetion of 3-bromoquinolines from α-bromo-β-arylaminoacrolein derivatives.

## EXPERIMENTAL

All melting points are uncorrected. $^1$H nmr spectra were recorded on JEOL PMX 60 and JEOL GX 400 nmr spectrometers with tetramethylsilane as an internal standard.

**2-Methyl-1-(*p*-methylphenylamino)-3-(*p*-methylphenylimino)-1-propene (1a), 2-Methyl-1-phenylamino-3-phenylimino-1-propene (1b) and 2-Methyl-1-(*p*-chlorophenylamino)-3-(*p*-chlorophenylimino)-1-propene (1c)** —— HCl salt of arylamine (0.01 mol) was dissolved in 10 ml of hot EtOH, and a solution of **2b** (0.005 mol) in 8 ml of EtOH and 2 ml of $H_2O$ were added to the solution. The solution was allowed to stand for 1 day at room temperature. The deposited crystals of HCl salt of **1** were collected and recrystallized from an appropriate solvent. The results were as follows (recrystallizing solvents are shown in parentheses). HCl salt of **1a** (MeOH): Yield 1.45 g. mp> 230°C [lit.,[11] mp (sublime)]. *Anal.* Calcd for $C_{18}H_{20}N_2 \cdot HCl$: C, 71.87; H, 7.04; N, 9.31. Found: C, 72.06; H, 7.08; N, 9.26. HCl salt of **1b** (MeOH): Yield 1.34 g. mp 231°C (dec.) [lit.,[11] mp 258°C and lit.,[12] mp 231°C (dec.)]. *Anal.* Calcd for $C_{16}H_{16}N_2 \cdot HCl \cdot 1/2MeOH$: C, 68.62; H, 6.63; N, 9.70. Found: C, 68.83; H, 6.37; N, 9.84. HCl salt of **1c** (EtOH): Yield 1.73 g. mp 237°C (dec.). *Anal.* Calcd for $C_{16}H_{14}Cl_2N_2 \cdot HCl \cdot 1/4\ H_2O$: C, 55.51; H, 4.51; N, 8.09. Found: C, 55.52; H, 4.29; N, 8.14.

HCl salt of **1** (0.01 mol) was added to a mixture of 200 ml of benzene and 50 ml of 10 % $Na_2CO_3$. The mixture was stirred until the whole changed into clear solutions. The benzene layer was dried over $K_2CO_3$, and concentrated under reduced pressure. The residue was recrystallized from 70 % EtOH. The results were as follows. **1a**: Yield 1.44 g (54 %). mp 165°C. *Anal.* Calcd for $C_{18}H_{20}N_2$: C, 81.78; H, 7.63; N, 10.60. Found: C, 81.67; H, 7.55; N, 10.56. $^1$H nmr ($CDCl_3$) δ: 7.46 (2H, s, 1,3-positions), 2.30 (6H, s, $CH_3$ of phenyl group) and 2.00 (3H, s, $CH_3$). **1b**: Yield 1.42 g (60 %). mp 139°C (lit.,[13] mp 136-138°C). *Anal.* Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85. Found: C, 81.16; H, 6.72; N, 11.53. $^1$H nmr ($CDCl_3$) δ: 7.62 (2H, s, 1,3-positions) and 2.00 (3H, s, $CH_3$). **1c**: Yield 1.90 g (62 %). mp 154°C. *Anal.* Calcd for $C_{16}H_{14}Cl_2N_2$: C, 62.97; H, 4.62; N, 9.18. Found: C, 62.91; H, 4.56; N, 8.96. $^1$H nmr ($CDCl_3$) δ: 7.57 (2H, s, 1,3-positions) and 2.00 (3H, s, $CH_3$).

**Hydrolysis of 1** —— A solution of AcOH (0.0005 mol) and AcONa (0.0045 mol) in 15 ml of $H_2O$ was added to a solution of **1** (0.005 mol) in 85 ml of EtOH. The mixture

was refluxed (**1a**: for 7 h; **1b**: for 4 h; 1c: for 4 h), and 0.1 g of $Na_2CO_3$ was added to the mixture. The whole was concentrated under reduced pressure. The precipitate was collected and recrystallized from 70 % EtOH. The results were as follows. **3a**: Yield, 0.71 g (81 %). mp 196°C. *Anal.* Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.25; H, 7.43; N, 8.23. $^1$H nmr ($CD_3SOCD_3$) δ: 9.00 (1H, s, CHO), 8.93 (1H, broad s, NH), 7.53 (1H, broad s, β-position), 2.20 (3H, s, $CH_3$ of phenyl group), 1.68 (3H, s, $CH_3$). **3b**: Yield, 0.75 g (93 %). mp 201°C (lit.,[3] mp 198-200°C). *Anal.* Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.22; H, 6.88; N, 8.86. $^1$H nmr ($CD_3SOCD_3$) δ: 9.04 (1H, d, $J$ = 13 Hz, NH), 9.03 (1H, s, CHO), 7.61 (1H, d, $J$ = 13 Hz, β-position) and 1.71 (3H, s, $CH_3$). **3c**: Yield, 0.88 g (90 %). mp 218°C. *Anal.* Calcd for $C_{10}H_{10}ClNO$: C, 61.39; H, 5.15; N, 7.16. Found: C, 61.49; H, 5.08; N, 6.93. $^1$H nmr ($CD_3SOCD_3$) δ: 9.07 (NH signal was overlapped with CHO signal), 7.62 (1H, s, β-position) and 1.70 (3H, s, $CH_3$).

**α-Ethyl-β-(*p*-toluidino)acrolein (4a) and α-Ethyl-β-anilinoacrolein (4b)** —— HCl salt of arylamine (0.005 mol) was dissolved in 8 ml of EtOH. A solution of **2c** (0.005 mol) in 4 ml of EtOH and 2 ml of $H_2O$ were added to the solution. The whole was allowed to stand for 50 min at room temperature, and 36 ml of $H_2O$ was added to the mixture. The precipitate was collected and recrystallized from 70 % EtOH. The results were as follows. **4a**: yield, 0.80 g (85 %). mp 135°C. *Anal.* Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.25; H, 8.16; N, 7.36. $^1$H nmr data are shown in Table 1. **4b**: Yield, 0.54 g (62 %). mp 123°C. *Anal.* Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.60; H, 7.81; N, 8.04. $^1$H nmr ($CD_3SOCD_3$) δ: 9.07 (1H, d, $J$ = 13 Hz, NH), 9.00 (1H, s CHO), 7.52 (1H, d, $J$ = 13 Hz, β-position), 2.32 (2H, q, $J$ = 7 Hz, $-C\underline{H}_2CH_3$) and 0.97 (3H, t, $J$ = 7 Hz, $-CH_2C\underline{H}_3$).

**α-Ethyl-β-(*p*-chloroanilino)acrolein (4c)** —— (1) 2-Ethyl-1-(*p*-chlorophenylamino)-3-(*p*-chlorophenylimino)-1-propene (**7c**) was prepared in the same manner as described for the preparation of **1**. HCl salt of **7c** (1.64 g, 88 %) was obtained from 0.01 mol of *p*-chloroaniline. *mp* >220°C. *Anal. Calcd for* $C_{17}H_{16}Cl_2N_2 \cdot HCl \cdot H_2O$: C, 54.64; H, 5.12; N, 7.50. Found: C, 54.40; H, 5.01; N, 7.20. The compound **7c** (2.58 g, 80 %) was obtained from 0.01 mol of HCl salt of **7c**. mp 98.5°C. *Anal.* Calcd for $C_{17}H_{16}Cl_2N_2 \cdot 1/4H_2O$: C, 63.07; H, 5.14; N, 8.65. Found: C, 63.24; H, 4.93; N, 8.49. $^1$H nmr ($CD_3SOCD_3$) δ: 7.62 (2H, broad s, 1-position), 2.42 ($-C\underline{H}_2CH_3$, this signal was overlapped with that of $CD_2H$ signal of the solvent) and 1.04 (3H, t, $J$ = 7 Hz,

$-CH_2\underline{C}H_3$). The compound **7c** was hydrolyzed in the same manner as described for hydrolysis of 1 to give 0.96 g (92 %) of **4c**. mp 190°C. *Anal.* Calcd for $C_{11}H_{12}ClNO$: C, 63.01; H, 5.77; N, 6.68. Found: C, 63.13; H, 5.73; N, 6.68. $^1$H nmr ($CD_3SOCD_3$) δ: 9.14 (1H, d, *J* = 12 Hz, NH), 9.01 (1H, s, CHO), 7.51 (1H, d, *J* = 12 Hz, β-position), 2.28 (2H, q, *J* = 7 Hz, $-C\underline{H}_2CH_3$) and 0.93 (3H, t, *J* = 7 Hz, $-CH_2\underline{C}H_3$).

(2) Five ml of 1 N HCl was added to a solution of 1.24 g (0.005 mol) of **2c** in 6 ml of EtOH, and the mixture was stirred for 1 h at room temperature. A solution of 1.36 g (0.01 mol) of $AcONa\cdot 3H_2O$ in 5 ml of $H_2O$ and a solution of 0.64 g (0.005 mol) of *p*-chloroaniline in 4 ml of EtOH were successively added to the mixture. The mixture was allowed to stand for 2 h at room temperature. The precipitate was filtered with suction. Twenty ml of $H_2O$ was added to the filtrate, and the second precipitate was collected. First precipitate contained a small amount of salt of **7c**, and was extracted with 70 ml of $CHCl_3$. The extract was concentrated under reduced pressure, and the residue was combined with the second precipitate, and the whole was recrystallized from 70 % EtOH to give 0.47 g (45 %) of **4c**.

**α-Phenyl-β-arylaminoacrolein** (**8**) —— HCl salt of arylamine (0.005 mol) was dissolved in 10 ml of EtOH. Twelve ml of $H_2O$ and 1.48 g (0.005 mol) of **2d** were added to the solution. The mixture was allowed to stand for 3 days at room temperature. The precipitate was collected and recrystallized from petroleum benzin to give **8**. The results were as follows. **8a**: Yield, 0.72 g (70 %). mp 148.5°C. *Anal.* Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.05; H, 6.37; N, 5.81. $^1$H nmr ($CDCl_3$) δ: 12.07 (d, *J* = 13 Hz, NH of s-*cis* form), 9.60 (d, *J* = 4 Hz, CHO of s-*cis* form), 9.30 (s, CHO of s-*trans* form), 7.57 (dd, *J* = 4, 13 Hz, β-position of s-*cis* form) and 2.32 (s, $CH_3$). **8b**: Yield, 0.65 g (59 %). mp 135°C. *Anal.* Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.37; H, 5.82; N, 6.08. $^1$H nmr ($CDCl_3$) δ: 12.00 (d, *J* = 13 Hz, NH of s-*cis* form), 9.50 (d, *J* = 4 Hz, CHO of s-*cis* form), 9.22 (s, CHO of s-*trans* form) and 7.50 (dd, *J* = 4, 13 Hz, β-position of s-*cis* form). **8c**: Yield, 0.82 g (78 %). mp 171°C. *Anal.* Calcd for $C_{15}H_{12}ClNO\cdot 1/4H_2O$: C, 68.71; H,4.81; N, 5.34. Found: C, 69.02; H, 4.55; N, 5.14. $^1$H nmr ($CDCl_3$) δ: 12.10 (d, *J* = 12 Hz, NH of s-*cis* form), 9.68 (d, *J* = 4 Hz, CHO of s-*cis* form), 9.40 (s, CHO of s-*trans* form) and 7.53 (dd, *J* = 4, 12 Hz, β-position of s-*cis* form).

**Recovery of 3-Methyl- and 3-Ethylquinolines from the Reaction Mixture in Which the Substrates were Heated with $AlBr_3$** —— A mixture of 0.004 mol of 3-methyl- or 3-ethylquinoline and 3.20 g (0.012 mol) of $AlBr_3$ was heated at 120°C for 5 h.

Twenty ml of $H_2O$ and 30 ml of 2 N NaOH were successively added to the mixture, and the mixture was extracted with ether. The ether layer was treated as usual to give respectively 0.49 g (87 %) of 3-methylquinoline and 0.55 g (96 %) of 3-ethylquinoline. The both samples were identical with authentic samples on the basis of comparison of their ir spectra and mixed melting point measurement of their picrates.

**Recovery of 3-Phenylquinoline from the Reaction Mixture in Which the Substrate was Heated with $AlBr_3$** —— A mixture of 0.62 g (0.003 mol) of 3-phenylquinoline and 2.40 g (0.009 mol) of $AlBr_3$ was heated at 120°C for 5 h. Ten ml of $H_2O$ and 20 ml of 2 N NaOH were successively added to the mixture, and the mixture was extracted with ether. The ether layer was dried over $K_2CO_3$, and concentrated under reduced pressure. The residue was subjected to PTLC (silica-gel) with benzene-AcOEt (5:1) to give 0.45 g (72 %) of 3-phenylquinoline. The sample was identical with authentic sample on the basis of comparison of their ir spectra.

**Cyclodehydration of 3, 4, 8a and 8b** —— A mixture of **3b** (0.48 g, 0.003 mol) and $AlBr_3$ (2.40 g, 0.009 mol) was heated at 120°C for 5 h. Ten ml of $H_2O$ and 30 ml of 2 N NaOH were added successively to the mixture. The whole was extracted with ether, and the ether layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The residue was purified by PTLC (silica-gel) with benzene-AcOEt (5:1) followed by distillation under reduced pressure to give 0.37 g (86 %) of 3-methylquinoline. The sample was identical with authentic sample on the basis of comparison of their ir spectra and mixed melting point measurement of their picrates (mp 186-189°C). The compounds **3a**, **3c**, **4**, **8a** and **8b** were cyclodehydrated in the same manner to give corresponding quinolines. The results are shown in Table 2.

3-Ethyl-6-chloroquinoline: mp 35°C. *Anal.* Calcd for $C_{11}H_{10}ClN$: C, 68.93; H, 5.26; N, 7.31. Found: C, 68.59; H, 5.15; N, 7.10. $^1H$ nmr ($CDCl_3$) δ: 8.63 (1H, d, $J$ = 2 Hz, 2-position), 2.80 (2H, q, $J$ = 7 Hz, $-\underline{CH_2}CH_3$) and 1.33 (3H, t, $J$ = 7 Hz, $-CH_2\underline{CH_3}$).

**Cyclodehdration of 8c** —— A mixture of **8c** (0.46 g, 0.0018 mol) and $AlCl_3$ (0.72 g, 0.0054 mol) was heated at 190-200°C for 5 h. Ten ml of $H_2O$ and 30 ml of 2 N NaOH were added successively to the mixture, and the whole was extracted with ether. The ether layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The residue was purified by PTLC (silica-gel) with benzene-AcOEt (5:1) followed by recrystallization from petroleum ether to give 0.22 g (28 %) of 3-phenyl-6-chloro-

quinoline. mp 104.5°C. *Anal.* Calcd for $C_{15}H_{10}ClN$: C, 75.16; H, 4.21; N, 5.84. Found: C, 75.29; H, 4.13; N, 5.72. $^1$H nmr ($CDCl_3$) δ: 9.07 (1H, d, $J$ = 2 Hz, 2-position) and 8.08 (1H, d, $J$ = 2 Hz, 4-position).

**Reaction of 5 and NBS** —— NBS (3.92 g, 0.022 mol) was added in portions to a solution of **5a** (5.01 g, 0.02 mol) in 40 ml of $CHCl_3$. The mixture was allowed to stand for 1 day at room temperature, and washed successively with two portions of 20 ml of 2 N NaOH and 20 ml of $H_2O$, and dried over $K_2CO_3$. The $CHCl_3$ layer was concentrated under reduced pressure. A small amount of EtOH was added to the residue, and the precipitate was collected and recrystallized from EtOH to give 4.55 g (69 %) of **10a**. mp 168°C (dec.) (lit.,[19] mp 164-165°C). $^1$H nmr ($CDCl_3$) δ: 7.93 (2H, s, 2-position) and 2.37 (6H, s, $CH_3$). The same treatment of 4.45 g (0.02 mol) gave 3.33 g (55 %) of **10b**. mp 147°C (dec.) (lit.,[19] mp 144-145°C). $^1$H nmr ($CDCl_3$) δ: 7.93 (2H, s, 2-position).

Table 2. Cyclodehydration of **3**, **4** and **8** in the Presence of Three Equivalent Amount of $AlBr_3$

| Starting Material | (mol) | Quinolines R$^1$ | R | Yields (%) | Recovered Starting Material (%) | mp (°C) | Picrate mp (°C) |
|---|---|---|---|---|---|---|---|
| **3a** | (0.002) | $CH_3$ | $CH_3$ | 65 | | 53[a] | 243[a] |
| **3c** | (0.0025) | Cl | $CH_3$ | 72 | 10 | 79[b] | 218 |
| **4a** | (0.002) | $CH_3$ | $C_2H_5$ | 82 | | | 248[c] |
| **4b** | (0.002) | H | $C_2H_5$ | 89 | | | 196.5[d] |
| **4c** | (0.002) | Cl | $C_2H_5$ | 81 | 5 | 35 | 217 |
| **8a** | (0.003) | $CH_3$ | $C_6H_5$ | 67 | | 61[e] | 248-249 (dec.) |
| **8b** | (0.002) | H | $C_6H_5$ | 51 | | 52[f] | 206[f] |

[a] lit.,[14] mp 56.5°C and picrate mp 251°C. [b] lit.,[15] mp 81-82°C. [c] lit.,[14] mp 247°C. [d] lit.,[14] mp 199°C. [e] lit.,[16] mp 63-64°C. [f] lit.,[17] mp 49-52°C and lit.,[18] mp 52°C and picrate mp 205°C.

**Hydrolysis of 10** —— A solution of 0.03 g (0.0005 mol) of AcOH and 0.61 g (0.0045 mol) of $AcONa \cdot 3H_2O$ in 15 ml of $H_2O$ was added to a solution of 1.65 g (0.005 mol) of **10a**. The mixture was refluxed for 3 h, and 20 ml of 7 % $NaHCO_3$ was added to the mixture. The whole was concentrated under reduced pressure, and the precipitate was collected and recrystallized from EtOH to give 1.03 g (86 %) of **9a**. mp 135°C. Reliquet, et al.[5] reported that melting point of **9a** is 130-133°C. They did not describe analytical and spectral data for the compound. *Anal.* Calcd for $C_{10}H_{10}BrNO$: C, 50.02; H, 4.20; N, 5.83. Found: C, 49.73; H, 4.01; N, 5.94. $^1H$ nmr ($CDCl_3$) δ: 9.30 (1H, s, CHO), 8.05 (1H, d, $J$ = 13 Hz, β-position) and 7.57 (1H, broad d, $J$ = 13 Hz, NH). The same treatment of 1.51 g (0.005 mol) of **10b** gave 0.90 g (80 %) of **9b**. mp 165°C. Reliquet, et al.[5] reported that melting point of **9b** is 164°C. They did not describe analytical and spectral data for the compoumd. *Anal.* Calcd for: $C_9H_8BrNO$: C, 47.81; H, 3.57; N, 6.20. Found: C, 47.42; H, 3.37; N, 6.26. $^1H$ nmr ($CDCl_3$) δ: 9.33 (1H, s, CHO), 8.07 (1H, d, $J$ = 13 Hz, β-position) and near 7.53 (NH, this signal overlapped with that of phenyl protons).

**Reaction of 6 and NBS** —— NBS (1.96 g, 0.011 mol) was added in portions to a solution of 1.61 g (0.01 mol) of **6a** in 10 ml of $CHCl_3$. The mixture was allowed to stand for 1 day at room temperature, and washed with two portions of 20 ml of $H_2O$. The $CHCl_3$ layer was dried over $K_2CO_3$, and concentrated under reduced pressure. The residue was recrystallized from EtOH to give 2.13 g (89 %) of **9a**. The same treatment of 1.47 g (0.01 mol) of **6b** gave 2.01 g (89 %) of **9b**.

**β-(2,4-Dibromoanilino)acrolein (12)** —— A solution of 1.10 g (0.01 mol) of β-ethoxyacrolein in 2 ml of AcOH and 13 ml of $H_2O$ were added to a solution of 2.51 g (0.01 mol) of 2,4-dibromoaniline in 24 ml of AcOH. The mixture was allowed to stand for 1 day at room temperature. The deposited yellow crystals were filtered with suction to give 1.55 g of crude **12**. The filtrate was concentrated under reduced pressure. The residue was extracted with petroleum benzin, and the petroleum benzin layer was concentrated under reduced pressure. The residue was combined with the above crude crystals of **12**, and the whole was recrystallized from petroleum benzin to give 2.21 g (73 %) of **12**. mp 128°C. *Anal.* Calcd for $C_9H_7Br_2NO$: C, 35.45; H, 2.31; N, 4.59. Found: C, 35.58; H, 2.07; N, 4.39.

**Reaction of 12 and NBS** —— NBS (0.39 g, 0.0022 mol) was added in portions to a solution of 0.16 g (0.002 mol) of **12** in 10 ml of $CHCl_3$. The mixture was allowed to stand for 2 days at room temperature. The deposited yellow crystals were filtered

with suction, and washed with $H_2O$ to remove contaminating succinimide, and recrystallized from EtOH to give 0.61 g (80 %) of **11**. mp 202°C. *Anal.* Calcd for $C_9H_6Br_3NO$: C, 28.16; H, 1.58; N, 3.65. Found: C, 28.24; H, 1.35; N, 3.58.

**Reaction of 9b and $AlBr_3$** —— (1) A mixture of 1.51 g (0.006 mol) of **9b** and 5.30 g (0.018 mol) of $AlBr_3$ was heated at 80°C for 30 min, and 20 ml of $H_2O$ was added to the mixture. The mixture was added in portions to 40 ml of 2 N NaOH under stirring, and the whole was extracted with two portions of 40 ml of $CHCl_3$. The $CHCl_3$ layer was extracted with 10 ml of 1 N HCl. The HCl layer was treated as usual to give a small amount of quinoline which was identical with authentic sample on the basis of comparison of their ir spectra. The $CHCl_3$ layer was dried over $K_2CO_3$, and concentrated under reduced pressure. Small amount of EtOH was added to the residue to give 0.25 g of **11** as a insoluble portion. The sample was identical with authentic sample (above section) on the basis of comparison of their ir spectra and mixed melting point measurement. EtOH soluble portion was subjected to PTLC (silica-gel) with benzene-AcOEt (6:1) to give a small amount of liquid. $^1H$ nmr pattern of the liquid was identical with that of 5,8-dibromoquinoline.

(2) A mixture of 1.51 g (0.006 mol) of **9b** and 5.30 g (0.018 mol) of $AlBr_3$ was heated at 120°C for 5 h and treated in the same manner as described for procedure (1) in this section. Quinoline (0.16 g) was obtained from the HCl layer. 5,8-Dibromoquinoline (0.05 g) and a small amount of 8-bromoquinoline were obtained from the $CHCl_3$ layer. The samples of 5,8-dibromoquinoline and 8-bromoquinoline were identical with authentic samples on the basis of comparison of their ir spectra.

**Reaction of 3-bromoquinoline and $AlBr_3$** —— A mixture of 2.10 g (0.01 mol) of 3-bromoquinoline and 8.00 g (0.03 mol) of $AlBr_3$ was heated at 120°C for 5 h, and 20 ml of $H_2O$ was added to the mixture. The mixture was added in portions to 70 ml of 2 N NaOH under stirring, and the whole was extracted with two portions of 30 ml of $CHCl_3$. The $CHCl_3$ layer was dried over $K_2CO_3$, and concentrated under reduced pressure. The residue was distilled under reduced pressure to give 1.62 g (73 %) of 3-bromoquinoline. The residue of distillation was subjected to PTLC (silica-gel) with benzene-AcOEt (5:1) to give 0.02 g of 3,5-dibromoquinoline which was identical with authentic sample on the basis of comparison of their ir spectra.

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