Abnormal Fischer Indolization and Its Related Compounds. XXII.[1] Fischer Indolization of Ethyl Pyruvate 2-(2-Chloro- and 2,6-Dichlorophenyl)methylhydrazones

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The Fischer indolization of ethyl pyruvate 2-(2-chlorophenyl)methylhydrazone (17) with HCl/EtOH proceeded rapidly to give six 1-methylindoles, ethyl 7-chloro (19), 6-chloro (22), and unsubstituted (24)-1-methylindole-2-carboxylates, and dichloro derivatives (21, 23, and 26), whereas no indolization had occurred with the corresponding NH-hydrazone, as described in a previous paper. This result shows that the abnormal Fischer indolization of 2-chlorophenylhydrazones with HCl/EtOH occurred in an *ortho*-C_6 fashion, in the same manner as that of the corresponding 2-methoxyphenylhydrazones (1 and 2).

The Fischer indolization of ethyl pyruvate 2-(2,6-dichlorophenyl)methylhydrazone (18) with HCl/EtOH did not occur at all, whereas the reaction with $ZnCl_2$/AcOH gave a low yield of ethyl 5,7-dichloro-3-methylindole-2-carboxylate (36), which was formed by migration of the *N*-methyl group during Fischer indolization.

Keywords Fischer indolization; 2-chlorophenylhydrazone; 2,6-dichlorophenylhydrazone; methyl group migration; ethanolic hydrogen chloride; indole

We reported[2] that the Fischer indolization of ethyl pyruvate 2-(2-methoxyphenyl)hydrazone (**1**) gave various abnormal indolic products, the formation of which depended on the kind of acid catalyst used. Typical effects of acid catalysts were that ethanolic hydrogen chloride (HCl/EtOH) gave ethyl 6-chloroindole-2-carboxylate (**3a**) (*ortho*-C_6 abnormal Fischer indolization), while $ZnCl_2$/AcOH gave the 5-chloroindole (**4**) (*ortho*-C_5 abnormal Fischer indolization), as the main abnormal products, respectively. The suggested mechanism involves the intermediate (**5**), which was formed by cyclization towards the position occupied by the methoxy group of the 2-methoxyphenylhydrazone (**1**). On the other hand, the corresponding 2-chloro- and 2,6-dichlorophenylhydrazones (**6** and **7**), also underwent the cyclization with zinc chloride in acetic acid ($ZnCl_2$/AcOH) to give the 5-chloroindoles (**4** and **8**), whereas no cyclization occurred with HCl/EtOH.

In relation to the Fischer cyclization of the 2-methoxyphenylhydrazone (**1**) we found[2a] that the corresponding N_α-methylhydrazone (**2**) also gave 6-substituted indoles (**3b** was a main product) on cyclization with HCl/EtOH. In addition to this fact, it should be noted that the reaction of the *N*-methylhydrazone (**2**) proceeded much more rapidly than that of the NH-hydrazone (**1**) under the same conditions. Generally, N_α-methylated arylhydrazones are known[3] to cyclize more readily than the corresponding NH-arylhydrazones. Recently, we also found[1] that the N_α-phenyl (aryl) group of phenylhydrazones has the same accelerating effect. This fact suggests that the chlorohydrazones (**6** and **7**), which did not cyclize with HCl/EtOH, would cyclize with this catalyst if a methyl group was introduced at the N_α-position, and thus we could examine abnormal Fischer indolization of 2-chlorophenylhydrazone with HCl/EtOH. In this paper we report the abnormal Fischer indolization of ethyl pyruvate 2-(2-chlorophenyl)- (**17**) and 2-(2,6-dichlorophenyl)- (**18**) methylhydrazones with HCl/EtOH.

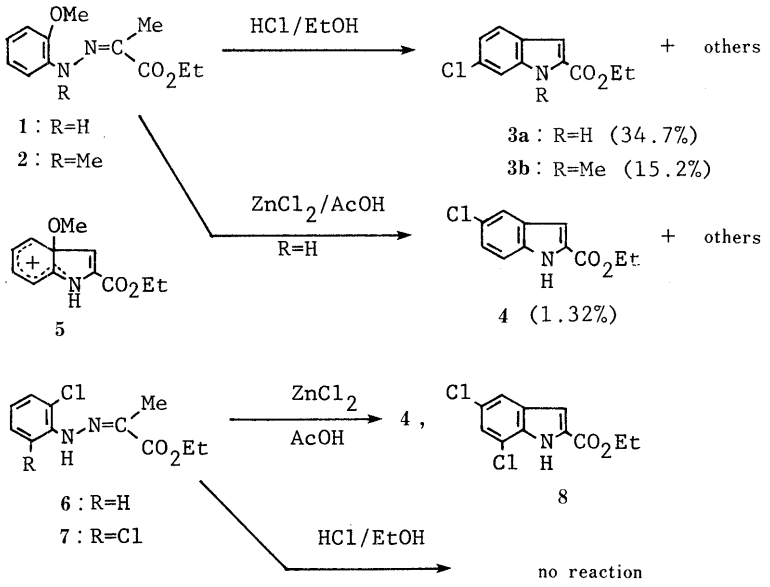


Chart 1

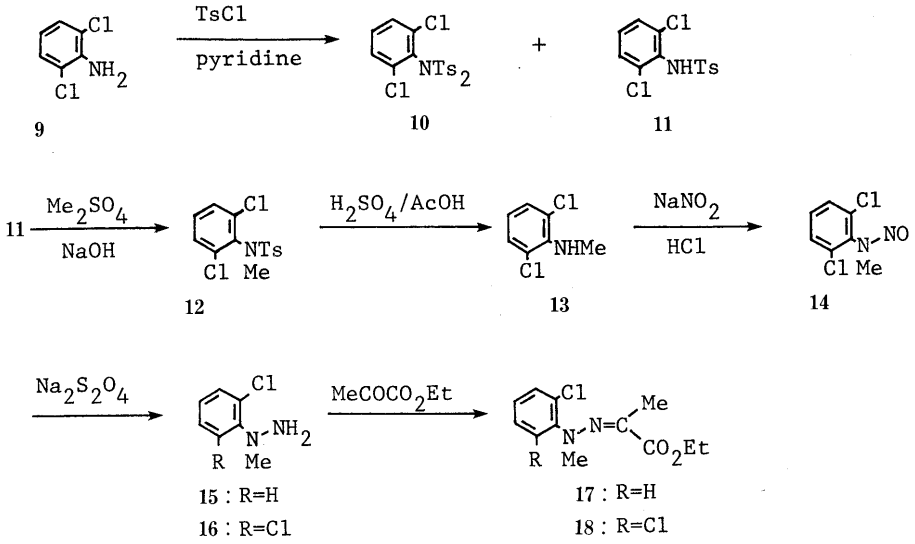
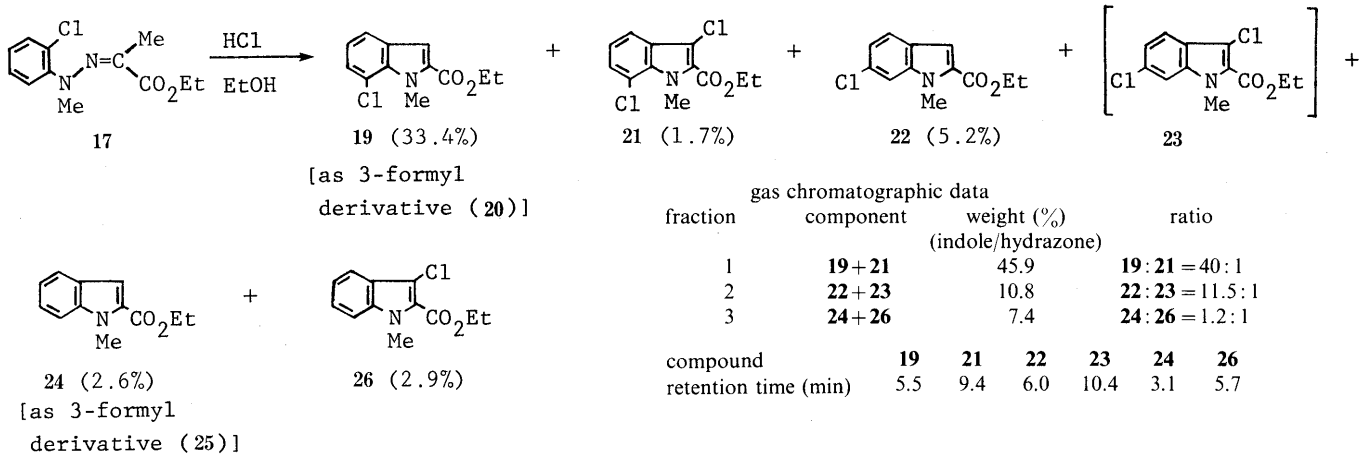


Chart 2



gas chromatographic data

fraction	component	weight (%) (indole/hydrazone)	ratio
1	**19**+**21**	45.9	**19**:**21** = 40:1
2	**22**+**23**	10.8	**22**:**23** = 11.5:1
3	**24**+**26**	7.4	**24**:**26** = 1.2:1

compound	**19**	**21**	**22**	**23**	**24**	**26**
retention time (min)	5.5	9.4	6.0	10.4	3.1	5.7

Chart 3

The chlorohydrazones (**17** and **18**) were prepared as follows. At first the 2-chlorohydrazone (**17**) was prepared by the condensation of known 1-(2-chlorophenyl)-1-methylhydrazine[4] (**15**) and ethyl pyruvate.

The dichlorohydrazone (**18**) was prepared starting from commercially available 2,6-dichloroaniline (**9**). Treatment of the aniline (**9**) with TsCl in pyridine gave the ditosylate (**10**) and the monotosylate (**11**). The latter (**11**) was methylated with dimethyl sulfate and then hydrolyzed with H_2SO_4 in AcOH to give 2,6-dichloro-*N*-methylaniline (**13**). Nitrosation of **13**, followed by reduction with $Na_2S_2O_4$ gave the hydrazine (**16**), which was, without purification, treated with ethyl pyruvate to give the desired ethyl pyruvate 2-(2,6-dichlorophenyl)methylhydrazone (**18**).

The reaction of the 2-chlorohydrazone (**17**) with HCl/EtOH proceeded smoothly as we had expected, and gave three spots on thin layer chromatography (TLC), all of which might be indolic products, because they were colored with Ehrlich reagent.[5] They were separated by column chromatography on silica gel. The melting points of these three fractions (fractions 1, 2, and 3), however, were not sharp, and gas chromatography showed that they were mixtures of two components, as Chart 3 shows.

Fraction 1 showed peaks at *m/z* 237 (corresponding to $C_{12}H_{12}ClNO_2$) and 271 ($C_{12}H_{11}Cl_2NO_2$, 11% intensity of *m/z* 237) in its mass spectrum (MS). The MS data suggested that fraction 1 consisted of ethyl *N*-methyl-monochlorinated indole-2-carboxylate and the corresponding dichlorinated compound. As no pure material could be obtained by recrystallization, Vilsmeier–Haack formylation was carried out on this mixture for their separation as 3-formyl derivatives. This reaction resulted in the formation of two separable compounds, **20** (mp 76.5—78 °C) and **21** (mp 84—85 °C).

Compound **20** was found to have the formula $C_{13}H_{12}ClNO_3$ by elemental analysis and MS. The infrared (IR) spectrum shows a carbonyl band at 1656 cm^{-1}. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum shows a singlet (1H) at δ 10.24 due to the formyl proton and a double doublet (1H, J=7.5 and 1.5 Hz) at δ 8.31 due to downfield-shifted C_4-H,[6] but no C_3-H. The splitting pattern of the C_4-H suggests that the chlorine substituent is located at the C_7-position of indole nucleus. These facts suggest that **20** is ethyl 7-chloro-3-formyl-1-methylindole-2-carboxylate, and thus the structure was established by comparison with an authentic sample, prepared from ethyl 7-chloro-1-methylindole-2-

carboxylate (**19**).

Compound **21** was found to have the formula $C_{12}H_{11}Cl_2NO_2$ by elemental analysis and MS. The IR spectrum shows no formyl band, and the ^{1}H-NMR spectrum shows neither formyl nor C_3-H. These data indicated that **21** is the dichloro compound formed from **19**, and the second chlorine should be located at the C_3-position. Thus **21** was suggested to be ethyl 3,7-dichloroindole-2-carboxylate and the structure was confirmed by comparison with an authentic sample, prepared from ethyl 7-chloroindole-2-carboxylate (**27**) (Chart 4).

The MS of fraction 2 shows the same two peaks at *m/z* 237 and 271 as those of fraction 1. Several recrystallizations of fraction 2 until the melting point reached a constant value (mp 75—76 °C) gave a pure product (**22**) having the formula $C_{12}H_{12}ClNO_2$. The splitting pattern of aromatic protons of this compound in the ^{1}H-NMR spectrum suggested that it is a 6-chloroindole derivative, and thus it was identified by comparison with an authentic sample of ethyl 6-chloro-1-methylindole-2-carboxylate[2a] (**22**). The other product in fraction 2 was not obtained in a pure state but was easily deduced to be a further chlorinated derivative of **22** at its 3-position on the basis of the constituents of fraction 1, and this was confirmed by comparison with an authentic sample of ethyl 3,6-dichloro-1-methylindole-2-carboxylate (**23**), prepared from ethyl 6-chloroindole-2-carboxylate (**3**), by gas chromatography.

Fraction 3 shows two main peaks at *m/z* 203 ($C_{12}H_{13}NO_2$) and 237 ($C_{12}H_{12}ClNO_2$) in the ratio of about 1 : 1, suggesting that they were ethyl 1-methylindole-2-carboxylate (**24**) and ethyl 3-chloro-1-methylindole-2-carboxylate (**26**). For structural confirmation, Vilsmeier–Haack reaction was carried out on fraction 3. This reaction yielded unreacted **26** and a formylated product (**25**). Compound **26** was identical with an authentic sample of ethyl 3-chloro-1-methylindole-2-carboxylate,[2a] and **25** with an authentic sample of ethyl 3-formyl-1-methylindole-2-carboxylate prepared according to the known method.[7]

The above result that the *N*-methyl-2-chlorophenylhydrazone (**17**) gave the 6-chloroindoles (**22** and **23**) revealed that the Fischer indolization of the NH-2-chlorophenylhydrazone (**6**) with HCl/EtOH could potentially occur in the same *ortho*-C_6 manner as that of the corresponding 2-methoxyphenylhydrazones[2a] (**1** and **2**). The reaction mechanism proposed in Chart 5, is essentially the same as that of the 2-methoxyphenylhydrazones[2a] (**1** and **2**). In this reaction three 3-chloroindoles (**21**, **23**, and **26**), which correspond to **19**, **22**, and **24**, respectively, were abnormally formed. Although the mechanism for the formation of these 3-chloroindoles is not clear, the following speculation would be one possibility. The formation of the dechlorinated indole (**24**) may be due to some reduction step[8] after formation of the intermediate (**30**). The reduction step should be inevitably accompanied by the oxidation step, by which the chloride anion is in turn oxidized to chlorine and attacks the reactive 3-position of the *N*-methylindoles already formed. The reduction step and the concurrent formation of chlorine may be visualized as shown in Chart 5 (**30**→**24**).

Next, the same hydrazone (**17**) was treated with $ZnCl_2$/AcOH, in order to examine the possibility of *ortho*-C_5 abnormal Fischer indolization. But the reaction was too fast to regulate, and gave a complex mixture from which no product could be isolated.

The Fischer indolization of the 2,6-dichlorohydrazone (**18**) was then investigated. Reaction of **18** with HCl/EtOH under reflux proceeded much more slowly than we had expected and was incomplete even after 6 h. In this reaction two products were obtained along with recovery of the starting hydrazone (**18**). One product was the hydrazine (**16**) which should be formed by ethanolysis of the hydrazone (**18**). The other (**32**) was found to have the formula $C_{17}H_{20}Cl_2N_2O_4$ by elemental analysis. In the MS a fragment ion at *m/z* 174 appeared as a base peak, while the parent peak did not appear at *m/z* 371 ($C_{17}H_{20}Cl_2N_2O_4$). In the ^{1}H-NMR spectrum the following groups were charac-

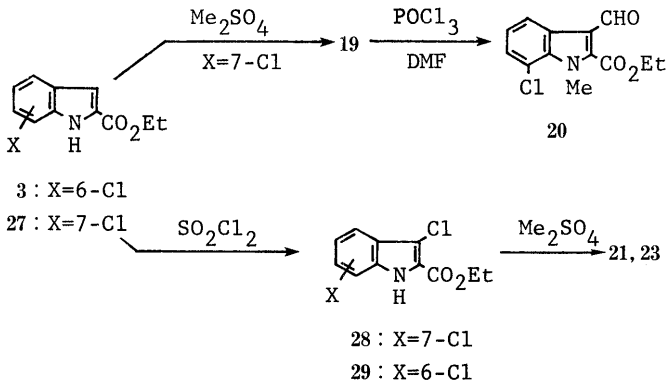


Chart 4

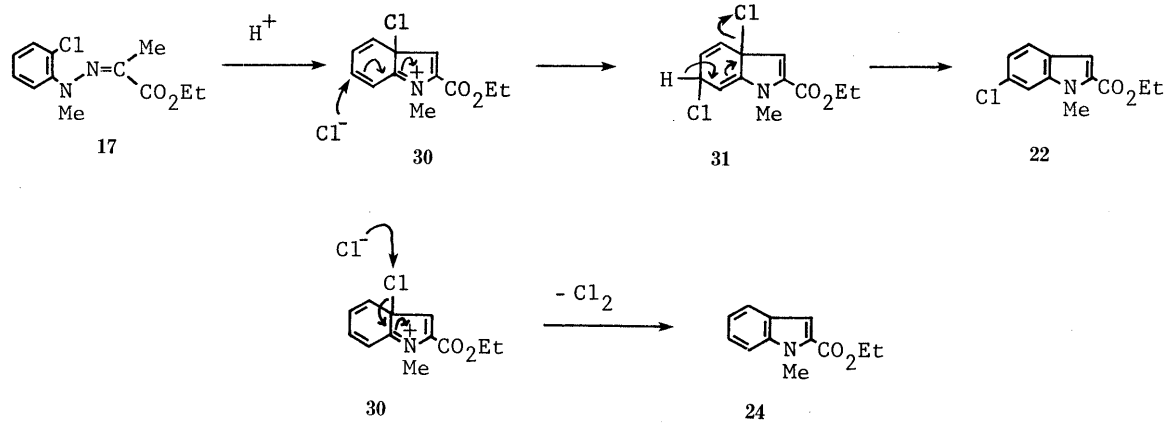


Chart 5

teristic; two ethoxy [δ 1.17 and 1.27 (each 3H triplet, CH_2CH_3), δ 3.47 and 4.24 (each 2H quartet, OCH_2CH_3)], *tert*-methyl [δ 1.65 (3H, s)], *N*-methyl [δ 3.53 (3H, s)], and vinylic proton [δ 6.36 (1H, s)]. On the basis of these data, we propose the structure of this compound as **32** in Chart 6, and the mechanism might be as follows (Chart 6). The dichlorohydrazone (**18**) coupled with the enol tautomer (**33**) of ethyl pyruvate, formed by ethanolysis of **18**, to afford the keto amide (**34**), which is transformed to the product (**32**) *via* ketalization and elimination of ethanol. This result showed that, in sharp contrast to **17**, no indolization occurred on the dichlorohydrazone (**18**) with HCl/EtOH.

In order to discriminate the difference of reactivity between the two hydrazones (**17** and **18**), the 2,6-dichlorohydrazone (**18**) was treated with $ZnCl_2$/AcOH, a more powerful acid catalyst than HCl/EtOH. With this catalyst the reaction proceeded slowly and gave an indolic compound (**36**), mp 164—166 °C, in 4.9% yield as a sole product with recovery of the starting hydrazone (**18**).

In analogy with the Fischer indolization of the NH-dichlorohydrazone[2b] (**7**), an expected indole from the *N*-methyl-dichlorohydrazone (**18**) was ethyl 5,7-dichloro-1-methylindole-2-carboxylate (**37**), mp 75—77 °C, which was prepared by methylation of ethyl 5,7-dichloroindole-2-carboxylate[2b] (**8**) for comparison. Although the product (**36**) was found to have the same formula $C_{12}H_{11}Cl_2NO_2$ as the 1-methylindole (**37**) and the ^{1}H-NMR spectrum shows two *meta*-coupled aromatic protons at δ 7.21 and 7.53 (each 1H, d, J=2.0 Hz), the two compounds were apparently different in spectra and physical constants. Reexamination of the spectra revealed that an NH-band appeared at 3320 cm^{-1} in the IR spectrum, and an aromatic methyl signal at δ 2.52 (3H, s) and NH at δ 8.83 (1H, br s, disappeared on addition of D_2O) in the ^{1}H-NMR spectrum. These data suggested that it was ethyl 5,7-dichloro-3-methylindole-2-carboxylate (**36**). The structure was confirmed by comparison with an authentic sample, which was in turn synthesized by the Fischer indolization of ethyl 2-oxobutyrate 2-(2,4-dichlorophenyl)hydrazone (**39**) prepared from 2,4-dichloroaniline (**38**) (Chart 7).

The mechanism for the formation of this abnormal product (**36**) is suggested to be as follows. The hydrazone (**18**) was converted to the ene-hydrazine tautomer (**41**) under acidic conditions. In this form, migration of the methyl group could occur and give a new hydrazone (**40**), which undergoes cyclization to the 3-methyl indole (**36**) in an usual manner. We know of no other report describing migration of the *N*-methyl group in phenylhydrazone to the carbon atom of its ene-hydrazine tautomer during the Fischer indolization. As described above, the 2-chloro-

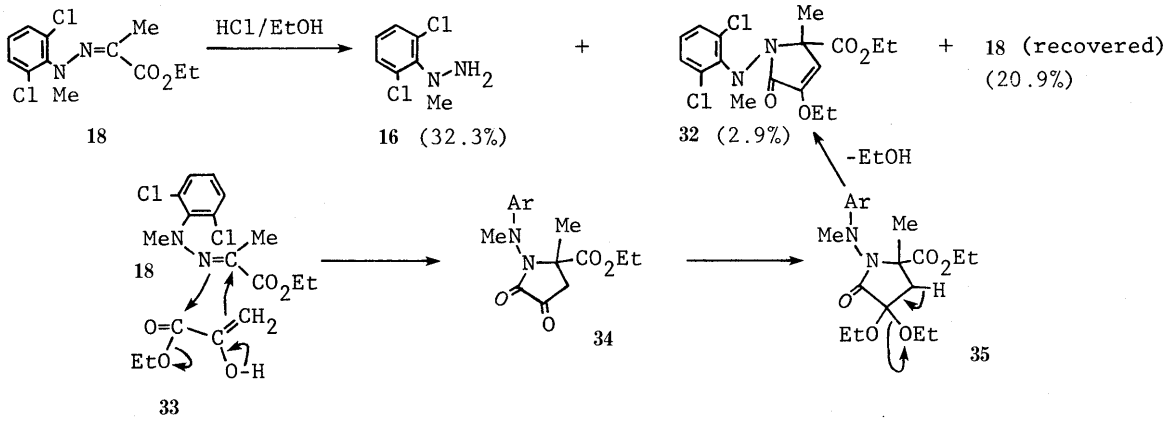


Chart 6

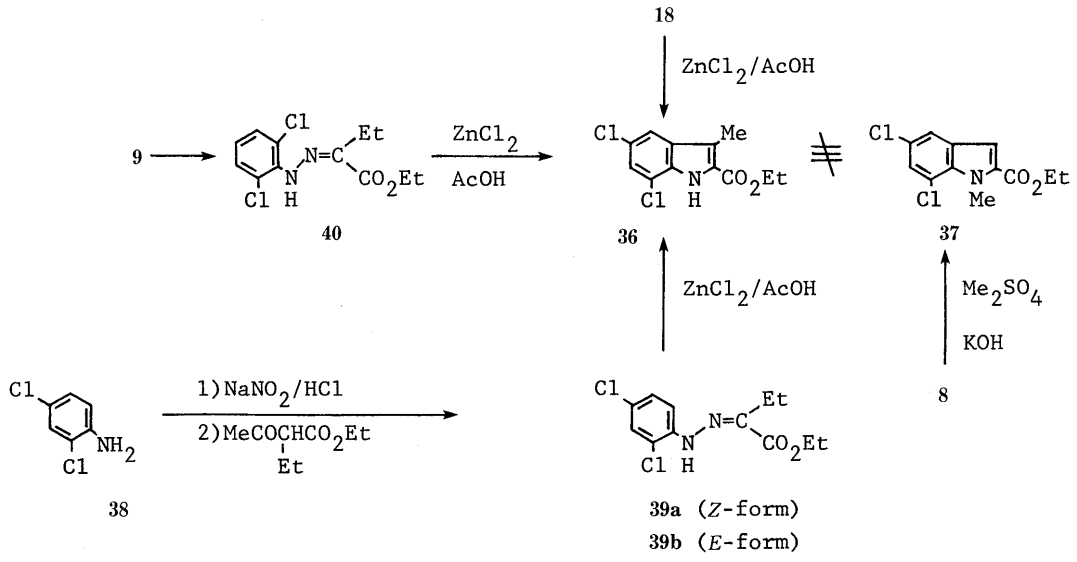


Chart 7

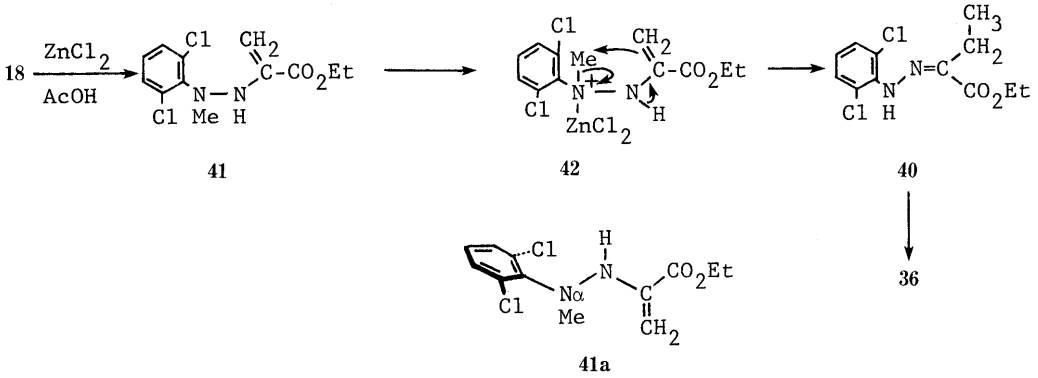


Chart 8

N-methylphenylhydrazone (**17**) cyclized with HCl/EtOH more easily than the corresponding NH compound as expected, whereas the 2,6-dichloro-*N*-methylphenylhydrazone (**18**) did not with HCl/EtOH. The latter hydrazone (**18**) should cyclize ultimately after migration of the *N*-methyl group, because the 5,7-dichloro-*N*-methylindole (**37**) was found to be recovered unchanged after heating with $ZnCl_2$/AcOH, the same conditions which caused conversion of the 2,6-dichlorohydrazone (**18**) into the 5,7-dichloro-3-methylindole (**36**). Thus, this phenomenon could be explained as follows; consideration of a Dreiding model of the ene-hydrazine (**41**) indicated that it would take the conformer (**41a**) as the most stable one, in which the N_α-methyl group is perpendicular to the plane of the 2,6-dichlorophenyl ring owing to steric repulsion between the methyl group and the chlorine atoms. This situation could not force the terminal carbon atom of the ene-hydrazine part to be close enough to the reacting site of the phenyl ring, but would be effective for the N_α-methyl group. In other words the ene-hydrazine part (**41**) would prefer to attack the N_α-methyl group by coordination of $ZnCl_2$ to the N_α atom to form the hydrazone (**40**). The resultant hydrazone (**40**) having no substituent interaction in the ene-hydrazine form would cyclize to give the indole (**36**). To confirm this point, ethyl 2-oxobutyrate 2-(2,6-dichlorophenyl)hydrazone (**40**) prepared from 2,6-dichloroaniline (**9**) by Japp–Klingemann reaction was submitted to the Fischer indolization with $ZnCl_2$/AcOH. The reaction proceeded smoothly and gave the expected indole (**36**) in good yield. Finally, these results are consistent with the hypothesis that for Fischer indolization the ene-hydrazine form of phenylhydrazone should take a specific conformation, in which all the atoms involved are suitably situated.

Experimental

All melting points were measured on a micro-melting point hot stage apparatus (Yanagimoto) and are uncorrected. IR spectra were obtained with a Hitachi EPI-G3 (in Nujol, unless otherwise stated). ^{1}H-NMR spectra were obtained with a JEOL JNM-MH-100 using tetramethylsilane as an internal standard (in $CDCl_3$, unless otherwise stated). MS were recorded on a Hitachi RMU-6E at 70 eV chamber voltage on a direct inlet system. Gas chromatography was done with a Hitachi gas chromatograph-063 equipped with a stainless steel column (1 m × 3 mm) packed with 10% SE-30. Conditions: column temperature, 180 °C; injection temperature, 180 °C; detection (FID) temperature, 175 °C; carrier gas, N_2 (30 ml/min). Silicic acid, 100 mesh, Mallinckrodt Chemical Works, was used for column chromatography. The terms singlet, doublet, double doublet, triplet, quartet, multiplet, and aromatic are abbreviated as s, d, dd, t, q, m, and Ar, respectively.

Ethyl Pyruvate 2-(2-Chlorophenyl)methylhydrazone (17) A solution of N_1-(2-chlorophenyl)-N_1-methylhydrazine[4] (**15**) (5.35 g) and ethyl pyruvate (3.95 g) in 60 ml of benzene containing a catalytic amount of TsOH was refluxed for 1.5 h. The reaction mixture was washed with dilute HCl and water, and dried over $MgSO_4$. The solvent was evaporated to give 8.01 g of an oil, which was purified by column chromatography on silicic acid (100 g) using benzene as the eluting solvent to afford 5.216 g of a pale yellow oil, bp 157 °C (2 mmHg), *Anal.* Calcd for $C_{12}H_{15}ClN_2O_2$: C, 56.58; H, 5.94; N, 11.00. Found: C, 56.47; H, 5.85; N, 11.18. IR ν_{max} cm^{-1}: no NH, 1707 (C=O). ^{1}H-NMR (CCl_4) δ: 1.35 (3H, t, J=7.3 Hz, CH_2CH_3), 1.54 (3H, s, N=C–CH_3), 3.29 (3H, s, NCH_3), 4.21 (2H, q, J=7.3 Hz), OCH_2CH_3), 6.93—7.48 (4H, m, Ar-H). MS *m/z*: 256 (M^++2, 36% intensity of M^+), 254 (M^+).

Ethyl Pyruvate 2-(2,6-Dichlorophenyl)methylhydrazone (18) i) 2′,6′-Dichloro-di-*p*-toluenesulfonanilide (10) and 2′,6′-Dichloro-*p*-toluenesulfonanilide (11) A cold solution of 2,6-dichloroaniline (**9**) (9.57 g) in 30 ml of pyridine was treated with TsCl (14.33 g) and the whole was refluxed for 5 h. The reaction mixture was poured into water and extracted with Et_2O. The organic layer was washed with 5% HCl and then water, dried over $MgSO_4$, and evaporated to dryness. The residue (19.21 g) was treated with cold benzene to give a benzene-insoluble solid and -soluble oil. The solid was recrystallized from ethanol–benzene to give 7.51 g (34.8%) of the disulfonanilide (**10**) as colorless needles, mp 256—258 °C. *Anal.* Calcd for $C_{20}H_{17}Cl_2NO_4S_2$: C, 51.07; H, 3.64; N, 2.98. Found: C, 50.88; H, 3.60; N, 3.01. IR ν_{max} cm^{-1}: 1160 (–SO_2N). ^{1}H-NMR δ: 2.44 (6H, s, 2 × Ar-CH_3), 7.20—7.40 (8H, m, Ar-H), 7.94 (4H, d, J=9.0 Hz, 2 × C_2-H and C_6-H).

The oil was crystallized by treating it with hexane and recrystallized from benzene–hexane to give 9.86 g (53.0%) of the monosulfonanilide (**11**) as colorless needles, mp 155–157 °C. *Anal.* Calcd for $C_{13}H_{11}Cl_2NO_2S$: C, 49.38; H, 3.51; N, 4.43. Found: C, 49.32; H, 3.50; N, 4.45. IR ν_{max} cm^{-1}: 3260 (NH), 1330, 1165 (–SO_2N). ^{1}H-NMR δ: 2.41 (3H, s, Ar-CH_3), 6.41 (1H, s, NH, disappeared by addition of D_2O), 7.20—7.36 (5H, m, Ar-H), 7.70 (2H, d, J=9.0 Hz, C_2-H and C_6-H). MS *m/z*: 317 (M^++2, 71% intensity of M^+), 315 (M^+).

ii) 2′,6′-Dichloro-*N*-methyl-*p*-toluenesulfonanilide (12) Dimethyl sulfate (13.2 ml) was added to a suspension of the monosulfonanilide (**11**) (5.69 g) in 44 ml of 4 N NaOH at room temperature, while keeping the mixture alkaline. When the addition was over, the reaction mixture was gently refluxed for 30 min. The separated crystals were filtered off and the filtrate was extracted with ether. The organic layer was dried over K_2CO_3 and evaporated to dryness. The resulting solid (5.67 g) was recrystallized from benzene–hexane to give 5.42 g (91.3%) of colorless needles, mp 119—121 °C. *Anal.* Calcd for $C_{14}H_{13}Cl_2NO_2S$: C, 50.92; H, 3.97; N, 4.24. Found: C, 50.77; H, 3.91; N, 4.27. IR ν_{max} cm^{-1}: 1140 (–SO_2N). ^{1}H-NMR δ: 2.43 (3H, s, Ar-CH_3), 3.18 (3H, s, NCH_3), 7.14—7.40 (5H, m, Ar-H), 7.78 (2H, d, J=9.0 Hz, C_2-H and C_6-H). MS *m/z*: 331 (M^++2, 74% intensity of M^+), 329 (M^+).

iii) 2,6-Dichloro-*N*-methylaniline[9] (13) Concentrated H_2SO_4 (5.6 ml) was added to a solution of the *N*-methylsulfonanilide (**12**) (4.39 g) in 2.5 ml of acetic acid, and the whole was heated at 80 °C for 2 h. The reaction mixture was made alkaline with 5% NaOH and extracted with ether. The organic layer was washed with water, dried over K_2CO_3, and evaporated to dryness *in vacuo*. The residual oil (1.86 g, 79.5%), bp 128—130 °C (27 mmHg), was used for the following reaction without further purification. IR ν_{max} cm^{-1}: 3400 (NH). ^{1}H-NMR δ: 3.02 (3H, s, NCH_3), 3.80 (1H, br s, NH, disappeared on addition of D_2O), 6.72 (1H, dd, J=9.0, 7.5 Hz, C_4-H), 7.19 (2H, d, J=8.0 Hz, C_3-H and C_5-H). MS *m/z*: 177

($M^+ + 2$, 67% intensity of M^+), 175 (M^+).

The *p*-nitrobenzoate of **13**: mp 182—183.5 °C from hexane. *Anal.* Calcd for $C_{14}H_{10}Cl_2N_2O_3$; C, 51.71; H, 3.10; N, 8.62. Found: C, 51.74; H, 3.09; N, 8.66. IR ν_{max}^{KBr} cm^{-1}: 1662 (C=O), 1521, 1351 (NO_2).

iv) 2,6-Dichloro-*N*-methyl-*N*-nitrosoaniline (14) A solution of $NaNO_2$ (599 mg) in 2.2 ml of water was added dropwise to a stirred solution of 2,6-dichloro-*N*-methylaniline (**13**) (1.5 g) in 1.2 ml of concentrated HCl at 0—3 °C and the whole was stirred for 1 h. The reaction mixture was poured into water, extracted with benzene, and dried over $MgSO_4$. Removal of the solvent gave 1.67 g of a solid, which was recrystallized from hexane to give 1.61 g (92.0%) of pale yellow prisms, mp 50—53 °C. *Anal.* Calcd for $C_7H_6Cl_2N_2O$: C, 41.00; H, 2.95; N, 13.66. Found: C, 41.04; H, 3.01; N, 13.44. IR ν_{max} cm^{-1}: 1433 (N–NO). ^{1}H-NMR δ: 3.34 ($3/5 \times 3H$,[10] s, CH_3–N–N=O), 4.09 ($2/5 \times 3H$,[10] s, CH_3–N–N=O), 7.30—7.59 (3H, m, Ar-H). MS *m/z*: 176 [$(M^+ - NO)+2$, 68% intensity of $(M^+ - NO)$], 174 ($M^+ - NO$, 25% of base peak).

v) Ethyl Pyruvate 2-(2,6-Dichlorophenyl)methylhydrazone (18) In a single portion, $Na_2S_2O_4$ (47.3 g) was added to a solution of the nitroso compound (**14**) (28.0 g) in 297 ml of 20% NaOH and 448 ml of ethanol at 58 °C under N_2. The mixture was stirred at 80 °C for 5 h, then poured into water, and extracted with ether. The organic layer was dried over K_2CO_3 and evaporated to dryness *in vacuo* to give the crude hydrazine (**16**) (19.1 g) as a pale yellow oil. A mixture of the hydrazine (**16**) (19.1 g) and ethyl pyruvate (11.5 g) in 500 ml of dry benzene was heated under reflux for 3 h using a Dean–Stark apparatus. The reaction mixture was washed with 1% HCl and dried over $MgSO_4$. The removal of the solvent gave a solid (23.0 g), which was recrystallized from benzene–hexane to give pale yellow needles (21.0 g, 53.2%), mp 48—50 °C. *Anal.* Calcd for $C_{12}H_{14}Cl_2N_2O_2$: C, 49.84; H, 4.88; N, 9.69. Found: C, 49.82; H, 4.81; N, 9.81. IR ν_{max} cm^{-1}: 1690 (C=O). ^{1}H-NMR δ: 1.33 (3H, t, J=7.0 Hz, $CH_2\underline{CH}_3$), 1.40 (3H, s, C–CH_3), 3.47 (3H, s, NCH_3), 4.27 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.20—7.40 (3H, m, Ar-H). MS *m/z*: 290 ($M^+ + 2$, 66% intensity of M^+), 288 (M^+).

Fischer Indolization of Ethyl Pyruvate 2-(2-Chlorophenyl)methylhydrazone (17) The hydrazone (**17**) (3.008 g) was dissolved in absolute ethanol (60 ml) saturated with HCl gas and refluxed for 20 min. The reaction mixture was concentrated *in vacuo* to about 30 ml, poured into 300 ml of water, and extracted with ether. The organic layer was washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$, and evaporated to dryness to give 2.671 g of an oil. The residual oil was chromatographed over silicic acid (120 g) with benzene–cyclohexane (2:3) as an eluting solvent to give three fractions: fraction 1, 1.380 g, mp 42.5—44.5 °C; fraction 2, 324 mg, mp 55—65 °C; fraction 3, 222 mg, mp 38—50 °C.

Fraction 1: The MS showed peaks at *m/z* 237 ($C_{12}H_{12}ClNO_2$) and *m/z* 271 ($C_{12}H_{11}Cl_2NO_2$, 11% intensity of *m/z* 237). This fraction was submitted to Vilsmeier–Haack reaction as follows. A solution of fraction 1 (1.380 g) in anhydrous dimethylformamide (DMF) (7 ml) was added to a solution of $POCl_3$ (4.25 g) in anhydrous DMF (15 ml). The whole was heated at 100—110 °C (bath) for 2 h, then poured into 200 ml of water, basified with 10% Na_2CO_3, and extracted with ether. The organic layer was washed with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give 1.501 g of a solid. Recrystallization from ethanol gave 657 mg of ethyl 7-chloro-3-formyl-1-methylindole-2-carboxylate (**20**) as colorless fine needles, mp 76.5—78 °C. *Anal.* Calcd for $C_{13}H_{12}ClNO_3$: C, 58.76; H, 4.55; N, 5.27. Found: C, 58.61; H, 4.49; N, 5.47. This sample was identical with an authentic sample of **20** described below.

The mother liquor of the recrystallization was evaporated and the resulting solid was chromatographed over silicic acid (30 g) with benzene as an eluting solvent. The first eluate gave 53 mg (1.7%) of ethyl 3,7-dichloro-1-methylindole-2-carboxylate (**21**), which was recrystallized from hexane to give colorless needles, mp 84—85 °C. This product was identical with an authentic sample of **21**.

The second eluate with the same solvent gave 458 mg of the 7-chloro-3-formylindole (**20**) [total yield: 1.115 g, 33.4% from the hydrazone (**17**)].

Fraction 2: Recrystallization from ethanol–water gave 146 mg (5.2%) of ethyl 6-chloro-1-methylindole-2-carboxylate (**22**) as fine needles, mp 75—76 °C. This product was identical with an authentic sample of **22**.[2a] The mother liquor was found to contain ethyl 3,6-dichloro-1-methylindole-2-carboxylate (**23**) by gas chromatography.

Fraction 3: The MS showed that the ratio of peaks at *m/z* 237 ($C_{12}H_{12}ClNO_2$) and 203 ($C_{12}H_{13}NO_2$) was 1.1:1. This fraction was submitted to Vilsmeier–Haack reaction as follows. A solution of 222 mg of fraction 3 in anhydrous DMF (1.5 ml) was added to a solution of $POCl_3$ (665 mg) in anhydrous DMF (4 ml), and the whole was heated at 100—115 °C (bath) for 2 h. The same work-up procedure as for fraction 1 gave 190 mg of a solid, which was chromatographed over silicic acid (10 g) with benzene as an eluting solvent. The first eluate gave 81 mg (2.9%) of ethyl 3-chloro-1-methylindole-2-carboxylate (**26**), which was recrystallized from hexane to give colorless needles, mp 70.5—71.5 °C. This product was identical with an authentic sample of **26**.[2c] The second eluate gave 66 mg (2.6% from **17**) of ethyl 3-formyl-1-methylindole-2-carboxylate (**25**), which was recrystallized from ethanol to give colorless columns, mp 114.5—116 °C. This product was identical with an authentic sample of **25**.[7]

Fischer Indolization of Ethyl Pyruvate 2-(2,6-Dichlorophenyl)methylhydrazone (18) with HCl in EtOH The hydrazone (**18**) (8.00 g) was dissolved in 80 ml of ethanol saturated with HCl and refluxed for 6 h. The reaction mixture was concentrated to about one-fourth of the original volume *in vacuo*, poured into water, and extracted with ether. The organic layer was washed with 5% HCl, dried over $MgSO_4$, and evaporated to give an oily residue (5.42 g)——fraction 1. The acidic aqueous solution was basified with 5% NaOH and extracted with ether. The organic layer was dried over K_2CO_3 and evaporated to give 2.12 g of an oily residue——fraction 2.

Fraction 1 was chromatographed over silicic acid (80 g) and eluted with benzene to give 1.67 g (20.9%) of the starting hydrazone (**18**). Further elution with $CHCl_3$ gave 0.42 g (2.9%) of ethyl 1-(2,6-dichloroanilino)-4-ethoxy-2-methyl-5-oxo-3-pyrroline-2-carboxylate (**32**), which was recrystallized from hexane to give pale yellow needles, mp 59.5—60.5 °C. *Anal.* Calcd for $C_{17}H_{20}Cl_2N_2O_4$: C, 52.72; H, 5.21; N, 7.23. Found: C, 52.67; H, 5.17; N, 7.03. IR ν_{max} cm^{-1}: 1710 (C=O). ^{1}H-NMR δ: 1.17 (3H, t, J=7.0 Hz, $CH_2\underline{CH}_3$), 1.27 (3H, t, J=7.0 Hz, $CH_2\underline{CH}_3$), 1.65 (3H, s, C–CH_3), 3.47 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 3.53 (3H, s, NCH_3), 4.24 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.36 (1H, s, vinylic H), 7.03—7.31 (3H, m, Ar-H). MS *m/z*: 176 [$(M^+ - C_{10}H_{14}NO_4)+2$, 63%], 174 ($M^+ - C_{10}H_{14}NO_4$, base peak).

Fraction 2 was purified by column chromatography over silicic acid (35 g) using $CHCl_3$ as an eluting solvent to give 1.71 g (32.3%) of the hydrazine (**16**).

Fischer Indolization of Ethyl Pyruvate 2-(2,6-Dichlorophenyl)methylhydrazone (18) with $ZnCl_2$ in AcOH Anhydrous $ZnCl_2$ (2.63 g) was added to a solution of the hydrazone (**18**) (1.05 g) in 12 ml of acetic acid, and the whole was refluxed for 1 h. The reaction mixture was poured into water and extracted with ether. The organic layer was dried over $MgSO_4$. Removal of the solvent gave 0.844 g of a residue, which was chromatographed over silicic acid (30 g) with benzene as an eluting solvent. The first eluate gave 48 mg (4.9%) of ethyl 5,7-dichloro-3-methylindole-2-carboxylate (**36**), which was recrystallized from benzene–hexane to give colorless needles, mp 160—162 °C. *Anal.* Calcd for $C_{12}H_{11}Cl_2NO_2$: C, 52.96; H, 4.07; N, 5.15. Found: C, 52.89; H, 4.01; N, 5.18. IR ν_{max} cm^{-1}: 3320 (NH), 1690 (C=O). ^{1}H-NMR δ: 1.42 (3H, t, J=7.0 Hz, $CH_2\underline{CH}_3$), 2.52 (3H, s, C_3-CH_3), 4.44 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.31 (1H, d, J=2.0 Hz, C_4-H or C_6-H), 7.53 (1H, d, J=2.0 Hz, C_6-H or C_4-H), 8.83 (1H, br s, NH, disappeared by addition of D_2O). MS *m/z*: 273 ($M^+ + 2$, 69% intensity of M^+), 271 (M^+). This sample was identical with an authentic sample of ethyl 5,7-dichloro-3-methylindole-2-carboxylate (**36**).

The second eluate with the same solvent gave 0.310 g (29.5%) of the starting hydrazone (**18**).

Preparations of Authentic Samples. Japp–Klingemann Reaction of 2,4-Dichloroaniline (38) with Ethyl α-Ethylacetoacetate A solution of 2,4-dichloroaniline (**38**) (10.0 g) in a mixture of concentrated HCl (16 ml) and water (25 ml) was treated with $NaNO_2$ (4.70 g) portionwise, and then AcONa (4.10 g) was added at 0 °C. A solution of ethyl α-ethylacetoacetate (9.80 g) in 62 ml of ethanol was basified with a solution of KOH (4.40 g) in water (6 ml) at 0 °C. To this solution was added the above diazonium salt solution at 0 °C, and the whole was stirred at 0 °C for 1 h. The reaction mixture was poured into water and extracted with ether. The organic layer was washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residual oil was treated with 10% H_3PO_4 in ethanol (62 ml) under reflux for 20 min. The reaction mixture was poured into water and extracted with ether. The organic layer was washed with water, dried over $MgSO_4$, and evaporated to dryness. The residual oil (18.86 g) was chromatographed over silicic acid (300 g) with benzene–cyclohexane (1:2) to give two eluates.

i) (*Z*)-Ethyl 2-Oxobutyrate 2-(2,4-Dichlorophenyl)hydrazone (39a) The product from the first eluate (9.10 g) was recrystallized from hexane to give yellow needles (8.43 g, 47.3%), mp 79.5—81 °C. *Anal.* Calcd for $C_{12}H_{14}Cl_2N_2O_2$: C, 49.84; H, 4.88; N, 9.69. Found: C, 49.94; H, 4.73; N, 9.90. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3270 (NH), 1680 (C=O). ^{1}H-NMR δ: 1.14 (3H, t,

J=7.0 Hz, $CH_2C\underline{H}_3$), 1.33 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 2.54 (2H, q, J=7.0 Hz, C–$C\underline{H}_2CH_3$), 4.28 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.15 (1H, dd, J=8.0, 3.0 Hz, C_5-H), 7.27 (1H, d, J=3.0 Hz, C_3-H), 7.52 (1H, d, J=8.0 Hz, C_6-H), 12.28 (1H, s, NH, disappeared by addition of D_2O). MS m/z: 290 (M^++2, 64.3% intensity of M^+), 288 (M^+).

ii) (*E*)-Ethyl 2-Oxobutyrate 2-(2,4-Dichlorophenyl)hydrazone (39b) The product from the second eluate (0.960 g) was recrystallized from hexane to give yellow needles (0.874 g, 4.9%), mp 109—110 °C. *Anal.* Calcd for $C_{12}H_{14}Cl_2N_2O_4$: C, 49.84; H, 4.88; N, 9.69. Found: C, 49.90; H, 4.82; N, 9.68. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (NH), 1710 (C=O). ^{1}H-NMR δ: 1.16 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 1.36 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 2.61 (2H, q, J=7.0 Hz, C–$C\underline{H}_2CH_3$), 4.30 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.18 (1H, dd, J=8.0, 3.0 Hz, C_5-H), 7.27 (1H, d, J=3.0 Hz, C_3-H), 7.57 (1H, d, J=8.0 Hz, C_6-H), 8.20 (1H, s, NH, disappeared on addition of D_2O). MS m/z: 290 (M^++2, 61% intensity of M^+), 288 (M^+).

Ethyl 5,7-Dichloro-3-methylindole-2-carboxylate (36) Anhydrous $ZnCl_2$ (2.55 g) was added to a solution of (*Z*)-ethyl 2-oxobutyrate 2-(2,4-dichlorophenyl)hydrazone (**39a**) (1.00 g) in 12 ml of acetic acid, and the whole was refluxed for 2 h. The reaction mixture was poured into water and extracted with ether. The organic layer was washed with water, dried over $MgSO_4$, and evaporated to dryness. The residue (0.958 g) was recystallized from benzene–hexane to give 0.821 g (87.2%) of colorless needles, mp 164—166 °C. *Anal.* Calcd for $C_{12}H_{11}Cl_2NO_2$: C, 52.96; H, 4.07; N, 5.15. Found: C, 52.92; H, 4.09; N, 5.10.

(*Z*)-Ethyl 2-Oxobutyrate 2-(2,6-Dichlorophenyl)hydrazone (40) 2,6-Dichloroaniline (**9**) (5.40 g) in 8.7 ml of concentrated HCl and 15 ml of water was diazotized with $NaNO_2$ (2.53 g) by the usual method. A solution of ethyl α-ethylacetoacetate (5.78 g) in 35 ml of ethanol was stirred, and a solution of KOH (2.40 g) in water (4 ml) was added, followed by the diazonium salt solution under ice-cooling. The whole was stirred for 30 min under ice-cooling, poured into water, and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated to dryness. The residue was dissolved in ethanol (35 ml) containing H_3PO_4 (3.5 g) and refluxed for 20 min. The whole was poured into water and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated to dryness. The residue (9.58 g) was chromatographed over silicic acid (120 g) and eluted with benzene to give 3.75 g (38.9%) of a solid, which was recrystallized from pentane to give pale yellow needles, mp 52.5—54 °C. *Anal.* Calcd for $C_{12}H_{14}Cl_2N_2O_2$: C, 49.84; H, 4.88; N, 9.69. Found: C, 49.62; H, 4.74; N, 9.30. IR ν_{max} cm^{-1}: 3215 (NH), 1695 (C=O). ^{1}H-NMR (CCl_4) δ: 1.17 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 1.38 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 2.54 (2H, q, J=7.0 Hz, C–$C\underline{H}_2CH_3$), 4.30 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.65—7.35 (3H, m, Ar-H), 11.95 (1H, br s, NH). MS m/z: 290 (M^++2, 71% intensity of M^+), 288 (M^+).

Further elution with benzene gave another oily product (2.24 g), but it could not be purified.

Ethyl 5,7-Dichloro-3-methylindole-2-carboxylate (36) from (*Z*)-Ethyl 2-Oxobutyrate 2-(2,6-Dichlorophenyl)hydrazone (40) Anhydrous $ZnCl_2$ (2.5 g) was added to a solution of the hydrazone (**40**) (0.500 g) in 10 ml of acetic acid, and the whole was refluxed for 1 h. The reaction mixture was poured into water and extracted with ether. The organic layer was washed with 5% $NaHCO_3$, dried over $MgSO_4$, and evaporated to dryness. The residue (448 mg) was chromatographed over silicic acid (15 g) and eluted with benzene to give a solid (369 mg, 78.4%). Recrystallization from benzene–hexane gave colorless needles, mp 166—167 °C. *Anal.* Calcd for $C_{12}H_{11}Cl_2NO_2$: C, 52.96; H, 4.07; N, 5.15. Found: C, 53.21; H, 4.08; N, 5.13.

General Procedure for *N*-Methylation of Ethyl Indole-2-carboxylate Derivatives A solution of ethyl indole-2-carboxylate derivative (2 mmol) in acetone (10 ml) was treated with 10% KOH (3 ml) and then dimethyl sulfate (2.5 mmol) at room temperature. The reaction mixture was stirred for 1—2 h, poured into water, and extracted with ether. The organic layer was dried over K_2CO_3 and evaporated to dryness. The residue was chromatographed over silicic acid and eluted with benzene to give the *N*-methylated compound. The yields were often low, because ester group hydrolysis also occurred. The resultant *N*-methyl carboxylic acid was not collected.

Ethyl 7-Chloro-1-methylindole-2-carboxylate (19) Ethyl 7-chloroindole-2-carboxylate[2b] (**27**) (448 mg) was methylated to give 134 mg (25.8%) of the product. Recrystallization from ethanol–water gave colorless needles, mp 39.5—41 °C. *Anal.* Calcd for $C_{12}H_{12}ClNO_2$: C, 60.64; H, 5.09; N, 5.89. Found: C, 60.57; H, 4.99; N, 5.99. IR ν_{max} cm^{-1}: 1722 (C=O). ^{1}H-NMR (CCl_4) δ: 1.38 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 4.29 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 4.44 (3H, s, NCH_3), 6.89 (1H, t, J=8.0 Hz, C_5-H), 7.13 (1H, s, C_3-H), 7.16 (1H, d, J=8.0 Hz, C_6-H), 7.42 (1H, d, J=8.0 Hz, C_4-H). MS m/z: 239 (M^++2, 33% intensity of M^+), 237 (M^+).

Ethyl 3,7-Dichloro-1-methylindole-2-carboxylate (21) i) Ethyl 3,7-Dichloroindole-2-carboxylate (28) A solution of ethyl 7-chloroindole-2-carboxylate[2b] (**27**) (500 mg) in 20 ml of anhydrous benzene was treated with SO_2Cl_2 (460 mg). The whole was gradually heated and then refluxed for 2.5 h. The solvent was removed *in vacuo* to give a solid (567 mg), which was chromatographed over silicic acid (15 g) and eluted with benzene to give the product (528 mg, 91.5%). Recrystallization from cyclohexane gave colorless needles, mp 128.5—129.5 °C. *Anal.* Calcd for $C_{11}H_9Cl_2NO_2$: C, 51.18; H, 3.51; N, 5.43. Found: C, 51.10; H, 3.50; N, 5.56. IR ν_{max} cm^{-1}: 3292 (NH), 1699 (C=O). ^{1}H-NMR (CCl_4) δ: 1.45 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 4.45 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 7.06 (1H, t, J=8.0 Hz, C_5-H), 7.29 (1H, d, J=8.0 Hz, C_6-H), 7.55 (1H, d, J=8.0 Hz, C_4-H), 9.07 (1H, br s, NH, disappeared by addition of D_2O). MS m/z: 259 (M^++2, 62% intensity of M^+), 257 (M^+).

ii) Ethyl 3,7-Dichloro-1-methylindole-2-carboxylate (21) Ethyl 3,7-dichloroindole-2-carboxylate (**28**) (130 mg) was methylated to give 45 mg (33%) of the product. Recrystallization from hexane gave colorless needles, mp 83—84.5 °C. *Anal.* Calcd for $C_{12}H_{11}Cl_2NO_2$: C, 52.96; H, 4.07; N, 5.15. Found: C, 52.90; H, 3.99; N, 5.31. IR ν_{max} cm^{-1}: 1713 (C=O). ^{1}H-NMR (CCl_4) δ: 1.44 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 4.36 (3H, s, NCH_3), 4.41 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 6.99 (1H, t, J=8.0 Hz, C_5-H), 7.25 (1H, dd, J=9.0, 1.5 Hz, C_6-H), 7.53 (1H, dd, J=8.0, 1.5 Hz, C_4-H). MS m/z: 273 (M^++2, 67% intensity of M^+), 271 (M^+).

Ethyl 3,6-Dichloro-1-methylindole-2-carboxylate (23) Ethyl 3,6-dichloroindole-2-carboxylate[11] (**29**) (260 mg) was methylated to give 213 mg (78%) of the product. Recrystallization from hexane gave colorless needles, mp 77.5—78.5 °C. *Anal.* Calcd for $C_{12}H_{11}Cl_2NO_2$: C, 52.96; H, 4.07; N, 5.15. Found: C, 52.95; H, 4.02; N, 5.45. IR ν_{max} cm^{-1}: 1700 (C=O). ^{1}H-NMR (CCl_4) δ: 1.44 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 3.98 (3H, s, NCH_3), 4.39 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 7.08 (1H, q, J=8.5, 2.5 Hz, C_5-H), 7.27 (1H, d, J=2.5 Hz, C_7-H), 7.55 (1H, d, J=8.5 Hz, C_4-H). MS m/z: 273 (M^++2, 66% intensity of M^+), 271 (M^+).

Ethyl 5,7-Dichloro-1-methylindole-2-carboxylate (37) Ethyl 5,7-dichloroindole-2-carboxylate (**8**) (518 mg) was methylated to give 351 mg (64.3%) of the product. Recrystallization from benzene–hexane gave colorless needles, mp 75—77 °C. *Anal.* Calcd for $C_{12}H_{11}Cl_2NO_2$: C, 52.96; H, 4.07; N, 5.15. Found: C, 52.86; H, 4.01; N, 5.15. IR ν_{max} cm^{-1}: 1709 (C=O). ^{1}H-NMR δ: 1.37 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 4.34 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.40 (2H, s, NCH_3), 7.16 (1H, s, C_3-H), 7.22 (1H, br s, C_4-H or C_6-H), 7.48 (1H, d, J=2.0 Hz, C_6-H or C_4-H). MS m/z: 273 (M^++2, 67% intensity of M^+), 271 (M^+).

Ethyl 3-Formyl-1-methylindole-2-carboxylate (25) A solution of ethyl 1-methylindole-2-carboxylate[12] (**24**) (222 mg) in 1.5 ml of anhydrous DMF was added to a solution of $POCl_3$ (0.50 g) in 3.5 ml of anhydrous DMF, and the whole was heated at 100—110 °C for 1 h. The reaction mixture was poured into water, basified with Na_2CO_3, and extracted with ether. The organic layer was washed with water and dried over $MgSO_4$. Removal of the solvent gave a solid (224 mg), which was chromatographed over silicic acid (20 g) and eluted with benzene to give 175 mg (69%) of the product. Recrystallization from ethanol gave colorles columns, mp 115—116.5 °C. *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.56; H, 5.69; N, 5.94. IR ν_{max} cm^{-1}: 1710 (C=O), 1648 (CHO). ^{1}H-NMR δ: 1.46 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 4.03 (3H, s, NCH_3), 4.49 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 7.22—7.50 (3H, m, Ar-H), 8.43—8.60 (1H, m, C_4-H), 10.56 (1H, s, CHO). MS m/z: 231 (M^+).

Ethyl 7-Chloro-3-formyl-1-methylindole-2-carboxylate (20) A solution of ethyl 7-chloro-1-methylindole-2-carboxylate (**19**) (77 mg) in 1 ml of anhydrous DMF was treated with a solution of $POCl_3$ (0.35 g) in 1 ml of anhydrous DMF in the same manner as described for the preparation of ethyl 3-formyl-1-methylindole-2-carboxylate (**25**) to give 62 mg (72%) of the product. Recrystallization from ethanol gave colorless fine needles, mp 76—77.5 °C. *Anal.* Calcd for $C_{13}H_{12}ClNO_3$; C, 58.76; H, 4.55; N, 5.27. Found: 58.91; H, 4.48; N, 4.91. IR ν_{max} cm^{-1}: no NH, 1720 (C=O), 1656 (CHO). ^{1}H-NMR (CCl_4) δ: 1.46 (3H t, J=7.5 Hz, $CH_2C\underline{H}_3$), 4.30 (3H, s, NCH_3), 4.46 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 7.07 (1H, t, J=7.5 Hz, C_5-H), 7.22 (1H, dd, J=7.5, 1.5 Hz, C_6-H), 8.31 (1H, dd, J=7.5, 1.5 Hz, C_4-H), 10.24 (1H, s, CHO). MS m/z: 267 (M^++2, 41% intensity of M^+), 265 (M^+).

References and Notes

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