[Chem. Pharm. Bull. 28(12)3639—3648(1980)]

Forced Nucleophilic Substitution Reaction of Chlorobenzenes bearing Electron-Donating Groups by the Use of "Naked" Methoxide Anion

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(Received July 9, 1980)

Nucleophilic aromatic substitution reactions of chlorobenzenes with the methoxide anion were found to proceed smoothly even in cases where electron-donating groups were present in the same aromatic ring when the chlorobenzenes were activated by chromium tricarbonyl complex formation and when the effectiveness of the methoxide anion was enhanced by the use of 18-crown-6. Application of the present method to indoline or tetrahydroquinoline systems was then examined and 5-chloro-1,3,3-trimethylindoline was successfully converted to the corresponding 5-methoxy or 5-benzyloxy compound.

Keywords——nucleophilic aromatic substitution; chromium tricarbonyl complex; "naked" methoxide anion; 18-crown-6; anisole derivatives; 5-methoxy-1,3,3-trimethylindoline

Many aromatic natural bases are known to possess mono-, di- or trimethoxy groups on the aromatic ring. In previous syntheses of these alkaloids, particularly in the syntheses of indole alkaloids, simple indole derivatives bearing an oxygen function at the required position have been used as starting materials. For example, 5-methoxyindole was used in the synthesis of iboga alkaloids[2] and 6-benzyloxy- and 6-methoxyindoles were used in the syntheses of reserpine[3] and vindoline,[4] respectively. However, the difficulty of obtaining sufficient amounts of particular starting materials has prevented the progress of synthetic studies of these oxygenated alkaloids. In order to find another practical route for syntheses of these alkaloids, we have investigated the introduction of a methoxy group into the aromatic ring of intermediates at a late stage of the syntheses,[5] in contrast with previous procedures.

To achieve this, it was initially necessary to establish a mild method which could be used in the presence of other functional groups in the same molecule. Chlorination followed by nucleophilic substitution of a methoxyl group for chlorine would be the method of choice if a suitable means for replacing chlorine by methoxyl could be developed. The activation of chlorobenzenes by the formation of chromium tricarbonyl complexes (CTC-complexes)[6,7] is quite promising, since a chromium tricarbonyl moiety is estimated to have an electron-

1) Location: *2-1 Hirosawa, Wako-shi, Saitama 351, Japan.*
2) G. Büchi, D.L. Coffen, K. Kocsis, P.E. Sonnet, and F.E. Ziegler, *J. Am. Chem. Soc.*, **88**, 3099 (1966).
3) R.B. Woodward, F.E. Bader, H. Bickel, A.J. Frey, and R.W. Kierstead, *Tetrahedron*, **2**, 1 (1958).
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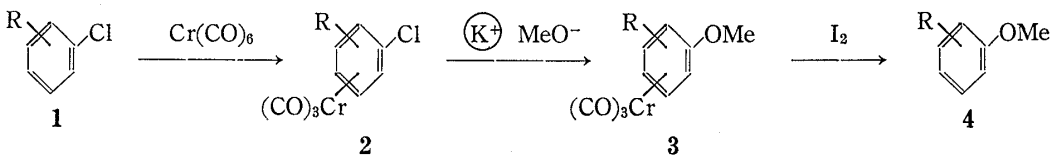
5) *a*) T. Oishi, M. Fukui, and Y. Endo, *Heterocycles*, **7**, 947 (1977); *b*) T. Hino, M. Taniguchi, A. Gonsho, and M. Nakagawa, *ibid.*, **12**, 1027 (1979); *c*) K. Saito and Y. Kikugawa, *J. Heterocycl. Chem.*, **16**, 1325 (1979).
6) *a*) B. Nicholls and M.C. Whiting, *J. Chem. Soc.*, **1959**, 551; *b*) D.A. Brown and J.R. Raju, *ibid.*, (A), **1966**, 40.
7) *a*) M.F. Semmelhack and H.T. Hall, *J. Am. Chem. Soc.*, **96**, 7091, 7092 (1974); *b*) M.F. Semmelhack, H.T. Hall, M. Yoshifuji, and G. Clark, *ibid.*, **97**, 1247 (1975); *c*) M.F. Semmelhack, H.T. Hall, Jr., and M. Yoshifuji, *ibid.*, **98**, 6387 (1976); *d*) M.F. Semmelhack, Y Thebtaranonth, and L. Keller, *ibid.*, **99**, 959 (1977); *e*) M.F. Semmelhack and G. Clark, *ibid.*, **99**, 1675 (1977); *f*) M.F. Semmelhack, G.R. Clark, R. Farina, and M. Saeman, *ibid.*, **101**, 217 (1979); *g*) M.F. Semmelhack, J. Bisaha, and M. Czarny, *ibid.*, **101**, 768 (1979); *h*) M.F. Semmelhack, H.T. Hall, Jr., R. Farina, M. Yoshifuji, G. Clark, T. Bargar, K. Hirotsu, and J. Clardy, *ibid.*, **101**, 3536 (1979).

withdrawing ability comparable to that of a nitro group[6,8] and can be removed readily when the substitution is completed. In fact, it has been reported that when CTC-chlorobenzene is refluxed for 24 hr with sodium methoxide in methanol, the corresponding CTC-anisole is obtained in high yield.[6] The release of anisole from the complex can be achieved by irradiation[9] or by oxidation with iodine[7] or ceric ammonium nitrate.[10] However, the substitution reactions should proceed in the presence of other electron-donating groups in the same aromatic ring in order for this method to be applicable to synthetic studies of natural products, since most natural bases inherently possess aniline type structures. We examined first whether the above method fulfilled this requirement or not, and found that no reaction took place when a methoxy group was present at the *ortho* position. However, this difficulty was readily overcome by activating the methoxide anion with the aid of crown ether.[11] The overall process for the introduction of a methoxy function into the aromatic ring is shown in Chart 1. The present paper describes the nucleophilic replacement of the chlorine atom of variously substituted chlorobenzenes and chlorinated simple heteroaromatic compounds with a methoxy group by means of the newly developed method.



R=H, Me, Me_2, OMe, NMe_2 and $(OMe)_2$

(K+) =K^+ trapped by 18-crown-6

Chart 1

The CTC-complexes of various chlorobenzene derivatives were prepared by heating $Cr(CO)_6$ with an excess of chlorobenzenes according to the reported procedure[6a,12] (Table I). The yields are not satisfactory, but are expected to be increased when an excess of $Cr(CO)_6$ is employed, as is shown in the cases of nitrogen-containing bicyclic systems (see below).

Tricarbonyl-η-(2-chloroanisole)chromium (CTC-2-chloroanisole, **2d**), a typical CTC-chlorobenzene derivative bearing an electron-donating group was subjected to reaction with potassium methoxide in methanol. The mixture was refluxed for 24 hr but no reaction occurred at all and the starting material was recovered unchanged. Semmelhack[7] has reported that when a nucleophile is sufficiently effective, even the hydrogen atom of CTC-benzenes can be replaced by that nucleophile. Based on these observations, we condsiered that the above difficulty might be associated with the rather weak nucleophilicity of the methoxide anion and thus the "naked" methoxide anion, reported to have an extremely high reactivity,[11] was used in place of simple sodium methoxide.

When CTC-chlorobenzene was allowed to react with 3 equiv. of potassium methoxide in the presence of 0.25 equiv. of 18-crown-6 in benzene or acetonitrile, the reaction was completed within 30 min at room temperature and CTC-anisole was obtained quantitatively. It should be recalled that without 18-crown-6, refluxing of the reaction mixture for 24 hr was necessary for the completion of the reaction.[6] The same technique was then applied to the reaction of the afore-mentioned CTC-chloroanisoles (**2d**, **e**, **f**: Entry 4, 5, 6) and this time, the

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11) D.J. Sam and H.E. Simmons, *J. Am. Chem. Soc.*, **96**, 2252 (1974).
12) W. Strohmeier, *Chem. Ber.*, **94**, 2490 (1961).

Table I. Preparation of CTC–Chlorobenzene Derivatives (1→2)

Entry	Compd.	R	Molar Ratio [Arene/ $Cr(CO)_6$]	Reaction Time (hr)	Yield[a] (%)	mp (°C)	Formula	Analysis (%)[e] Calcd (Found) C	H	Cl	N
1	**2a**	H	10	100	66	104—105[c]	$C_9H_5ClCrO_3$				
2	**2b**	2-Me	10	75	54	101—102	$C_{10}H_7ClCrO_3$	45.73 (45.78	2.68 2.74	13.50 13.23)	
3	**2c**	4-Me	8	95	74	91—92[d]	$C_{10}H_7ClCrO_3$				
4	**2d**	2-OMe	8	72	44	108—110	$C_{10}H_7ClCrO_4$	43.11 (43.50	2.53 2.57	12.72 12.03)	
5	**2e**	3-OMe	5	95	51	86—87	$C_{10}H_7ClCrO_4$	(43.28	2.61	12.44)	
6	**2f**	4-OMe	5	55	26	66—67	$C_{10}H_7ClCrO_4$	(43.69	2.65	11.53)	
7	**2g**	3,4-Me_2	5	75	28	72—73	$C_{11}H_9ClCrO_3$	47.76 (49.23	3.28 3.53	12.81 10.79)	
8	**2h**	2,5-Me_2	5	95	39	74—75	$C_{11}H_9ClCrO_3$	(48.25	3.49	11.99)	
9	**2i**	3-NMe_2	3	95	61	165—166 (dec.)	$C_{11}H_{10}ClCrNO_3$	45.30 (45.24	3.45 3.46	12.15 12.09	4.80 4.89)
10	**2j**	4-NMe_2	0.5	79	21	115—116	$C_{11}H_{10}ClCrNO_3$	(45.39	3.55	12.01	4.74)
11	**2k**	2,5-$(OMe)_2$	4	95	40[b]	—	$C_{11}H_9ClCrO_5$				

a) Calculated from the amount of consumed $Cr(CO)_6$.
b) The yield is less than 40% because substantial amounts of CTC-1,4-dimethoxybenzene are involved in this complex.
c) Lit.,[6a] mp 102—103°
d) Lit.,[13] mp 87—90°.
e) CTC–Chlorobenzenes **2d, f, g, h, k** did not give satisfactory elemental analytical data because these compounds were contaminated with small amounts of dechlorinated CTC–complexes. However, CTC–anisole derivatives **3** derived from these compounds were found to be sufficiently pure after one recrystallization (see Table II).

Table II. Substitution Reactions by "Naked" Methoxide Anion (2→3)

Entry	Compd.	R	18-Crown-6 (equiv)	Conditions[a]	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N
1	**3a**	H	0.25	25°, 0.5 hr	100	85—86[c]	$C_{10}H_8CrO_4$			
2	**3b**	2-Me	0.25	60°, 1.5 hr	97	74—75[d]	$C_{11}H_{10}CrO_4$			
3	**3c**	4-Me	0.25	60°, 0.75 hr	99	56—57[e]	$C_{11}H_{10}CrO_4$			
4	**3d**	2-OMe	0.25	60°, 1.0 hr	94	116—117[f]	$C_{11}H_{10}CrO_5$			
5	**3e**	3-OMe	0.25	60°, 0.75 hr	99	127—128[g]	$C_{11}H_{10}CrO_5$			
6	**3f**	4-OMe	0.25	60°, 1.5 hr	96	100—101[h]	$C_{11}H_{10}CrO_5$			
7	**3g**	3,4-Me_2	0.33	60°, 2.0 hr	98	84—86	$C_{12}H_{12}CrO_4$	52.94 (52.82	4.44 4.46)	
8	**3h**	2,5-Me_2	0.33	60°, 1.75 hr	98	73—74	$C_{12}H_{12}CrO_4$	(52.90	4.44)	
9	**3i**	3-NMe_2	0.33	70°, 1.0 hr	97	122—123	$C_{12}H_{13}CrNO_4$	50.18 (50.10	4.56 4.55	4.87 4.82)
10	**3j**	4-NMe_2	0.50	70°, 3.0 hr	93	106—107	$C_{12}H_{13}CrNO_4$	(50.02	4.59	4.85)
11	**3k**	2,5-$(OMe)_2$	0.50	70°, 3.5 hr	[b]	[b]	$C_{12}H_{12}CrO_6$			

a) All reactions were carried out using 3 equiv. of potassium methoxide in benzene under an atmosphere of nitrogen.
b) See the experimental section.
c) Lit.,[6a] mp 86—87°.
d) Lit.,[6a] mp 75—77°.
e) Lit.,[6a] mp 52—52.5°.
f) Lit.,[14] mp 116°.
g) Lit.,[14] mp 122°.
h) Lit.,[14] mp 101°.

13) H.P. Fritz and C.G. Kreiter, *J. Organomet. Chem.*, **7**, 427 (1967).
14) W. McFarlane and S.O. Grim, *J. Organomet. Chem.*, **5**, 147 (1966).

expected CTC-dimethoxybenzenes (**3d**, **e**, **f**: Entry 4, 5, 6) were obtained in more than 94% yields, although somewhat severe conditions (60°, 45—90 min) were necessary in these cases.

In the same way, other CTC-chlorobenzenes bearing electron-donating groups underwent substitution of methoxyl for chlorine in high yields, as summarized in Table II.

Removal of the chromium tricarbonyl moiety proceeded in essentially quantitative yields when the tetrahydrofuran (THF) solutions were treated with an excess of iodine. In the cases where amino groups are present in the complexes (**3i**, **j**: Entry 9, 10), unidentified products were obtained on iodine treatment. However, their formation, which was presumed to be related to the presence of a basic center, was completely avoided when dilute hydrochloric acid was added to the THF solution before iodine addition.

Encouraged by the above findings that even *m*- and *p*-(*N*,*N*-dimethylamino)chlorobenzenes can be convertible to the corresponding anisoles, we examined whether or not the present method is applicable to nitrogen-containing bicyclic systems. 5-Chloroindoline (**6a**)[15] and 6-chloro-1,2,3,4-tetrahydroquinoline (**6b**)[16] were chosen as simple examples first. These compounds were prepared in good yields from 1-acetyl **5a** and **5b** by chlorination with sulfuryl chloride followed by deacetylation with acid by the reported procedure.[16] CTC-Complex formation was then carried out with an excess of $Cr(CO)_6$. When 5-chloroindoline was refluxed with 2 equiv. of $Cr(CO)_6$ in diglyme–cyclohexane (1: 1) at 125° for 70 hr under an atmosphere of nitrogen, the corresponding CTC-complex **7a** was obtained as yellow crystals in 68% yield. Even under these severe conditions, the starting material **6a** remained partially unchanged but could be recovered cleanly by extraction with dilute hydrochloric acid from the reaction mixture (recovered, 16%). These CTC-complexes are insoluble in 10% HCl, which shows that the basicity of the amino groups was greatly decreased by CTC-complex formation. In the same way, CTC-6-chloro-1,2,3,4-tetrahydroquinoline (**7b**) was obtained in 50% yield (85% yield, calculated from the consumed starting material).

As was presumed from the reduced basicity of **7a** and **7b**, base-catalyzed hydrogen abstraction from secondary amines took place readily. Therefore, the masking of these nitrogens should be necessary before base treatment. Addition of **7a** to a benzene suspension of 1.3 equiv. of potassium hydride followed by benzyl bromide treatment at room temperature afforded the 1-benzyl derivative **9a** in 92% yield after silica-gel chromatography. In this case, the addition of a catalytic amount of 18-crown-6 again remarkably facilitated the reaction. The CTC-complex **9a** was then treated with 4 equiv. of potassium methoxide in the presence of 0.5 equiv. of 18-crown-6. The reaction was completed after only 3 hr at 70° and the corresponding methoxy derivative **11a** was obtained as pale yellow needles in 92% yield after purification. Subsequent oxidative cleavage of the chromium tricarbonyl moiety by treatment with iodine in THF/10%HCl afforded, within 30 min at room temperature, 1-benzyl-5-methoxyindoline (**13a**). Similarly, 5-methoxy-1-methylindoline (**12a**), 6-methoxy-1-methyl-1,2,3,4-tetrahydroquinoline (**12b**) and 1-benzyl-6-methoxy-1,2,3,4-tetrahydroquinoline (**13b**) were obtained in three steps (N-protection, chlorine substitution, and iodine treatment) in good yields.

1,3,3-Trimethyloxindole and indoline were then chosen as model compounds of naturally occurring 3,3-disubstituted oxindole or indoline·alkaloids and the introduction of an oxygen function at the 5-position was investigated.

5-Chloro-1,3,3-trimethyloxindole (**15**) was prepared from 1,3,3-trimethyloxindole (**14**)[17] by N-chlorosuccinimide treatment or from 3,3-dimethyloxindole (**16**)[18] by chlorination with

15) R. Ikan, E. Hoffmann, E.D. Bergmann, and A. Galum, *Israel J. Chem.*, **2**, 37 (1964).
16) R.D. Gano, R.L. McKee, and J.W. Ager, *J. Am. Chem. Soc.*, **74**, 3176 (1952).
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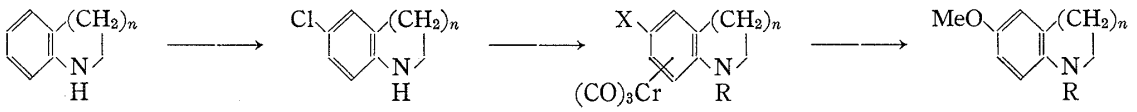
18) K. Brunner, *Monatsh. Chem.*, **18**, 95 (1897).



5a, b **6a, b** **7a, b:** X=Cl, R=H **12a, b:** R=Me

8a, b: X=Cl, R=Me **13a, b:** R=CH_2Ph

9a, b: X=Cl, R=CH_2Ph

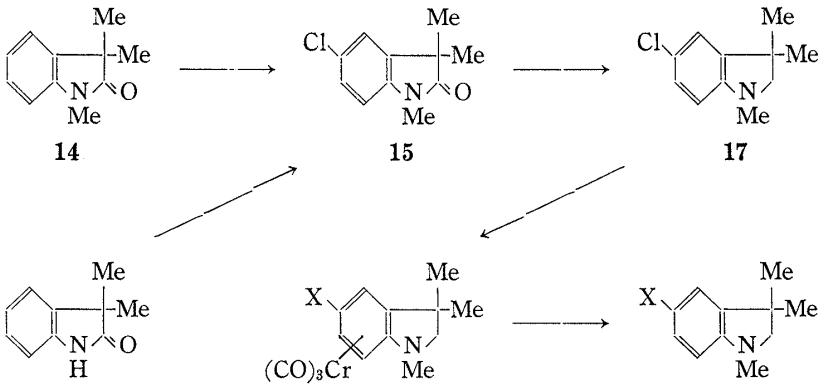
a: $n=1$ **10a, b:** X=OMe, R=Me

b: $n=2$ **11a, b:** X=OMe, R=CH_2Ph

Chart 2

1-chlorobenzotriazole[19] followed by N-methylation. Formation of CTC-5-chloro-1,3,3-trimethyloxindole was initially attempted, but even if **15** was refluxed for 2 days with an excess of $Cr(CO)_6$ in diglyme-cyclohexane, no reaction occurred at all. However, the indoline **17** derived from **15** by $LiAlH_4$ reduction gave the corresponding CTC-complex **18** in 50% yield under the same reaction conditions. The subsequent nucleophilic substitution reaction took place quite smoothly when the CTC-complex **18** was allowed to react with "naked" methoxide or benzyloxide anion in the same way as noted for the preparation of **10** and **11**. Oxidative decomposition of the resulting complexes **19a, b** produced the methoxy or benzyloxy indolines **20a, b** in high yields, as expected.

We were confronted with difficulty in forming CTC-complexes when the substrates were extended to tricyclic 5-chloroindoline derivatives, which shows that the present method is of limited use in effecting our primary purpose. However, once CTC-chlorobenzenes were formed, replacement of chlorine with alkoxyl was found to proceed surprisingly smoothly with the aid of 18-crown-6, even if electron-donating groups were present in the same molecule. Therefore, the present method should still be quite useful in the preparation of various types of otherwise rather inaccessible alkoxy benzene derivatives.



14 **15** **17**

16 **18** : X=Cl **20a:** X=OMe

19a: X=OMe **20b:** X=OCH_2Ph

19b: X=OCH_2Ph

Chart 3

Experimental

All melting points were taken in open capillaries with a Mitamura Riken melting point apparatus (type 1—128, No. 146) and are uncorrected. IR spectra were measured on a Hitachi 215 spectrophotometer, NMR spectra on Varian HA-100D and JEOL C-60HL instruments, and MS spectra on a Hitachi RMU-6MG mass spectrometer.

Preparation of CTC-Chlorobenzene Derivatives 2——Compound **2a** was prepared by a modification of Strohmeier's method[12]; $Cr(CO)_6$ (10 g, 45.5 mM) was added to a solution of chlorobenzene (45 ml) in diglyme

19) C.W. Rees and R.C. Storr, *Chem. Commun.*, **1968**, 1305.

(45 ml) and cyclohexane (45 ml) and the mixture was heated for 100 hr under reflux (bath temp.: 125—130°) under an atmosphere of nitrogen. $Cr(CO)_6$ that sublimed inside the reflux condenser was sometimes returned mechanically to the reaction flask. The solution was then diluted with ether and filtered through alumina. The solvents were evaporated off and the orange residue was triturated with hexane. The resulting yellow solids were collected by filtration and washed with hexane to give 7.5 g of yellow powder (**2a**, 66% yield). Recrystallization from ether–hexane furnished yellow prisms, mp 104—105°. The CTC-chlorobenzenes **2b**—**2k** were prepared in the manner described for the preparation of **2a**. Reaction times, yields and melting points are shown in Table I. Spectral data (IR and NMR) are shown in Table III.

Aromatic Substitution Reactions of CTC-chlorobenzenes 2a—2k with "Naked" Methoxide Anion——18-Crown-6 (50 mg, 0.25 equiv.) was added to a suspension of well-powdered potassium methoxide (150 mg, 3 equiv.) in dry benzene (15 ml) under nitrogen and the mixture was gradually heated to 60°. After 30 min, CTC-2-chloroanisole (**2d**, 200 mg) was added all at once and the whole was stirred for 1.0 hr at 60°. The solution was passed through a short column of silica-gel with benzene as an eluent. Removal of the solvent gave **3d** as a yellow solid (185 mg, 94% yield), which was recrystallized from ether–hexane to afford light yellow needles, mp 116—117°. Other CTC-anisoles **3a—c**, **3e—j** were prepared in the same way except for **3k**; the reaction conditions, yields and melting points are shown in Table II. Spectral data are listed in Table IV.

CTC-1,2,4-Trimethoxybenzene (**3k**)——Crude CTC-2,5-dimethoxychlorobenzene (**2k**, 350 mg) containing CTC-1,4-dimethoxybenzene was treated with "naked" methoxide anion for 3.5 hr at 70° in benzene, and the crude product was purified by silica-gel chromatography with CH_2Cl_2–benzene (1 : 1) as an eluent to afford CTC-1,4-dimethoxybenzene (**3f**, 100 mg) and CTC-1,2,4-trimethoxybenzene (**3k**, 140 mg). **3k** was obtained as a yellow viscous oil, although the same compound was previously reported to be a crystalline compound of mp 114°.[14] However, the structure of **3k** was confirmed by the quantitative liberation of 1,2,4-trimethoxybenzene (**4k**) upon iodine treatment.

Release of Free Arene Ligands from CTC-Complexes——CTC-Complexes **3a—h** and **3k** were treated with an excess of iodine in THF at room temperature for 30 min. After the addition of 20%$NaHSO_3$ solution, free arenes were extracted with ether and the solvents were dried over $MgSO_4$. The structures of the free arenes **4a—h** and **4k** thus obtained were confirmed by direct comparison of their IR spectra with those of authentic samples.

3-(*N*,*N*-Dimethylamino)anisole (**4i**)——CTC-Complex **3i** (195 mg) was dissolved in a mixture of THF (5 ml) and 10%HCl (5 ml), and then iodine (680 mg) in THF (2 ml) was added dropwise to this solution. The whole was stirred for 30 min at room temperature. In order to remove excess iodine, 20%$NaHSO_3$ was added until the solution turned green, then the solution was made alkaline by the addition of 20%NaOH. The mixture was extracted with ether and the extract was dried over $MgSO_4$ and concentrated to give a yellow oil (108 mg), which was chromatographed on alumina. Elution with ether afforded **4i** as a colorless

Table III. Spectral Data for CTC–Chlorobenzenes

Compd.	IR νcm^{-1} (nujol) (C≡O)	IR νcm^{-1} (nujol) (Ar–O and/or Ar–N)	NMR δ (d_6-acetone) (* in $CDCl_3$)
2a	1993, 1960, 1870		*4.83—5.16 (1H, m, Ar–H), 5.42 (4H, d, J=3.0 Hz, Ar–H)
2b	1988, 1960, 1918, 1860		2.36 (3H, s, CH_3), 5.34—6.00 (4H, m, Ar–H)
2c	1993, 1983, 1960, 1920, 1870		*2.09 (3H, s, CH_3), 5.25 (2H, d, J=7.0 Hz, Ar–H), 5.50 (2H, d, J=7.0 Hz, Ar–H)
2d	1990, 1962, 1890	1520	*3.84 (3H, s, OCH_3), 4.90—5.44 (3H, m, Ar–H), 5.79 (1H, d, J=6.4 Hz, Ar–H)
2e	1992, 1960, 1919, 1870	1530	3.86 (3H, s, OCH_3), 5.24—5.50 (2H, m, Ar–H), 5.78 (1H, m, Ar–H), 5.98 (1H, t, J=6.6 Hz, Ar–H)
2f	1985, 1970, 1918, 1850	1530	3.76 (3H, s, OCH_3), 5.57 (2H, d, J=7.2 Hz, Ar–H), 6.09 (2H, d, J=7.2 Hz, Ar–H)
2g	1986, 1950, 1910, 1875		2.14 (3H, s, CH_3), 2.30 (3H, s, CH_3), 5.32—5.96 (3H, m, Ar–H)
2h	1984, 1945, 1910		2.23 (3H, s, CH_3), 2.29 (3H, s, CH_3), 5.30—5.92 (3H, m, Ar–H)
2i	1940, 1855, 1835	1550	3.02 (6H, s, NMe_2), 4.89—5.41 (3H, m, Ar–H), 5.91 (1H, t, J=7.2 Hz, Ar–H)
2j	1940, 1830	1550	2.92 (6H, s, NMe_2), 5.15 (2H, d, J=7.2 Hz, Ar–H), 6.03 (2H, d, J=7.2 Hz, Ar–H)
2k	1945, 1860		3.74 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 5.32 (1H, dd, J=2.4 and 7.2 Hz, Ar–H), 5.82—5.97 (2H, m, Ar–H)

Table IV. Spectral Data for CTC–Anisoles

Compd.	IR νcm^{-1} (nujol) (C≡O)	IR νcm^{-1} (nujol) (Ar–O and/or Ar–N)	NMR δ (d_6-acetone) (* in $CDCl_3$)
3a	1985, 1950, 1910, 1860	1535	*3.68 (3H, s, OCH_3), 4.81—5.61 (5H, m, Ar–H)
3b	1975, 1950, 1850	1540, 1520	2.16 (3H, s, CH_3), 3.83 (3H, s, OCH_3), 5.18 (1H, m, Ar–H), 5.49—5.85 (3H, m, Ar–H)
3c	1985, 1950, 1850	1550	2.10 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 5.47 (2H, d, J=7.2 Hz, Ar–H), 5.76 (2H, d, J=7.2 Hz, Ar–H)
3d	1955, 1835	1540, 1530	*J4.04 [6H, s, $(OCH_3)_2$], 5.26—5.66 (4H, m, Ar–H)
3e	1965, 1945, 1850	1550, 1525	3.85 [6H, s, $(OCH_3)_2$], 5.16 (2H, dd, J=2.2 and 7.0 Hz, Ar–H), 5.52 (1H, t, J=2.2 Hz, Ar–H), 5.94 (1H, t, J=7.0 Hz, Ar–H)
3f	1940, 1855	1556, 1527	3.72 [6H, s, $(OCH_3)_2$], 5.65 (4H, s, Ar–H)
3g	1970, 1895, 1850	1514	2.15 (3H, s, CH_3), 2.32 (3H, s, CH_3), 3.83 (3H, s, OCH_3), 5.08—5.70 (3H, m, Ar–H)
3h	1974, 1940, 1900, 1860	1552	2.12 (3H, s, CH_3), 2.24 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 5.05 (1H, d, J=6.0 Hz, Ar–H), 5.54 (1H, br s, Ar–H), 5.84 (1H, d, J=6.0 Hz, Ar–H)
3i	1940, 1840	1560, 1526	2.94 (6H, s, NMe_2), 3.75 (3H, s, OCH_3), 4.63—5.03 (3H, m, Ar–H), 5.73 (1H, t, J=6.8 Hz, Ar–H)
3j	1940, 1850	1560, 1520	2.83 (6H, s, NMe_2), 3.66 (3H, s, OCH_3), 5.19 (2H, d, J=7.5 Hz, Ar–H), 5.60 (2H, d, J=7.5 Hz, Ar–H)
3k	1955, 1860 (neat)	1560, 1535	

oil (100 mg, 99%). IR ν_{max}^{neat} cm^{-1}: 1610, 1580 (Ar). NMR δ (CCl_4): 2.87 (6H, s, NMe_2), 3.67 (3H, s, OCH_3), 6.01—6.27 (3H, m, Ar–H), 6.79 (1H, m, Ar–H).

4-(*N*,*N*-Dimethylamino)anisole (4j)——In the manner described for **4i**, **4j** was obtained as a pale yellow solid, mp 49—50° (lit.,[20] mp 47°). NMR δ (CCl_4): 2.81 (6H, s, NMe_2), 3.66 (3H, s, OCH_3), 6.63 (4H, s, Ar–H).

5-Chloroindoline (6a)——1-Acetylindoline (6.0 g) was dissolved in CCl_4 (150 ml) and SO_2Cl_2 (6.0 g) was added dropwise to this solution, keeping the temperature below 25° by ice cooling. When the mixture had been stirred for 1 hr at room temperature, the precipitated white solid was dissolved by the addition of CH_2Cl_2. Water was added to this mixture and the organic layer was separated, washed with 20%NaOH and dried over $MgSO_4$. Removal of the solvents gave a pale yellow solid (7.0 g), which was dissolved in EtOH (40 ml) and heated to reflux. Conc.HCl (40 ml) was added to this solution and the whole was refluxed for another 3 hr. EtOH was evaporated off and the aqueous layer was washed with ether, and made alkaline by the addition of 20%NaOH. The free base was extracted with ether. The extract was dried over $MgSO_4$ and concentrated to give a black oil (5.25 g), which was chromatographed on silica-gel. Elution with EtOAc–benzene (1: 1) gave 5-chloroindoline (4.9 g, 71% from 1-acetylindoline). Distillation of the crude **6a** gave a colorless oil, bp 83—84° (3.5 Torr) [lit.,[15] bp 132—135° (20 Torr)]. IR ν_{max}^{neat} cm^{-1}: 3375 (NH), 1608 (Ar). NMR δ (CCl_4): 2.69—3.70 (4H, m), 3.49 (1H, s, NH), 6.32 (1H, d, J=8.4 Hz, C_7–H), 6.72—7.00 (2H, m, Ar–H). MS m/e: 155 (M^++2), 153 (M^+), 117 (M^+−HCl).

6-Chloro-1,2,3,4-tetrahydroquinoline (6b)——Compound **6b** was obtained in 58% yield from 1-acetyl tetrahydroquinoline in the manner noted for the preparation of **6a**. **6b**: white crystals, bp 65—67° (0.05 Torr), mp 39—40° [lit.,[16] bp 125—127° (3 Torr), mp 41°]. IR ν_{max}^{neat} cm^{-1}: 3410 (NH), 1603, 1580 (Ar). NMR δ (CCl_4): 1.73—1.99 (2H, m), 2.66 (2H, t, J=6.8 Hz), 3.21 (2H, t, J=5.7 Hz), 3.55 (1H, s, NH), 6.17 (1H, d, J=9.2 Hz, C_8–H), 6.68—6.86 (2H, m, Ar–H). MS m/e: 169 (M^++2), 167 (M^+).

CTC-5-Chloroindoline (7a)——A solution of 5-chloroindoline (**6a**, 1.53 g) and $Cr(CO)_6$ (4.4 g, 2 equiv.) in diglyme (20 ml) and cyclohexane (20 ml) was refluxed for 70 hr at 125° under nitrogen. The mixture was cooled to room temperature under nitrogen, then ether was added and the solution was filtered through alumina. The organic layer was washed with cold 10%HCl three times and then with water three times, dried over $MgSO_4$ and concentrated to give an orange oil, which was chromatographed on silica-gel. Elution with EtOAc–benzene (2: 3) afforded **7a** as a yellow solid (1.97 g, 68%), which was recrystallized from ether–hexane to give yellow prisms, mp 107—108°. IR ν_{max}^{Nujol} cm^{-1}: 3420 (NH), 1945, 1880, 1830 (C≡O), 1560, 1510 (Ar–N). NMR δ (d_6-acetone): 2.70—3.10 (2H, m), 3.20—3.82 (2H, m), 5.16 (1H, d, J=6.6 Hz, C_7–H), 5.74 (1H, dd, J=1.7 and 6.6 Hz, C_6–H), 6.02 (1H, d, J=1.7 Hz, C_4–H). *Anal.* Calcd for $C_{11}H_8ClCrNO_3$: C, 45.61;

20) D.P. Evans, H.B. Watson, and R. Williams, *J. Chem. Soc.*, **1939**, 1345.

H, 2.78; Cl, 12.24; N, 4.83. Found: C, 46.15; H, 2.85; Cl, 11.55; N, 4.79. The HCl layer was made alkaline by the addition of 20%NaOH and was extracted with ether. The ether layer was dried over $MgSO_4$ and concentrated to give 240 mg of the starting material **6a** (16%).

CTC-6-Chloro-1,2,3,4-tetrahydroquinoline (**7b**)——In the manner noted for the preparation of **7a**, **7b** was obtained in 50% yield (85% yield, calculated from the consumed starting material **6b**) as yellow prisms (from ether–hexane), mp 121—122°. IR ν_{max}^{Nujol} cm^{-1}: 3390 (NH), 1940, 1875, 1853, 1832 (C≡O), 1560, 1524 (Ar–N). NMR δ (d_6-acetone): 1.76—2.14 (2H, m), 2.44—3.38 (5H, m), 5.09 (1H, d, J=7.2 Hz, C_8–H), 5.80 (1H, dd, J=1.8 and 7.2 Hz, C_7–H), 5.97 (1H, d, J=1.8 Hz, C_5–H). *Anal.* Calcd for $C_{12}H_{10}ClCrNO_3$: C, 47.46; H, 3.31; Cl, 11.67; N, 4.61. Found: C, 47.65; H, 3.39; Cl, 10.88; N, 4.53.

N-Alkylation of CTC-Complexes 7a, b with Methyl Iodide and Benzyl Bromide: CTC-5-Chloro-1-methylindoline (**8a**)——18-Crown-6 (136 mg, 0.25 equiv.) was added to a suspension of potassium hydride[21] (215 mg, 1.3 equiv.) in dry benzene (20 ml) and the mixture was stirred for 30 min at room temperature. CTC-5-Chloroindoline (**7a**, 600 mg) in benzene (10 ml) was added dropwise to this suspension. After 30 min, methyl iodide (0.17 ml, 1.3 equiv.) was added. The mixture was stirred for another 30 min and then filtered through silica-gel to remove the crown ether and inorganic salts. The filtrate was concentrated and the resulting crude product was chromatographed on silica-gel. Elution with CH_2Cl_2-benzene–hexane (2:2:1) gave 530 mg (84%) of **8a** and 50 mg (8%) of the starting material **7a**. The crude **8a** was recrystallized from ether–hexane to give yellow prisms of mp 88—89°. IR ν_{max}^{Nujol} cm^{-1}: 1975, 1956, 1937, 1850 (C≡O), 1550 (Ar–N). NMR δ (d_6-acetone): 2.64 (3H, s, NCH_3), 2.68—3.80 (4H, m), 5.10 (1H, d, J=6.8 Hz, C_7–H), 5.74 (1H, dd, J=1.6 and 6.8 Hz, C_6–H), 5.97 (1H, d, J=1.6 Hz, C_4–H). *Anal.* Calcd for $C_{12}H_{10}ClCrNO_3$: C, 47.76; H, 3.32; Cl, 11.67; N, 4.61. Found: C, 47.57; H, 3.33; Cl, 11.64; N, 4.49. The compounds **8b**, **9a**, and **9b** were prepared in the same way.

CTC-6-Chloro-1-methyl-1,2,3,4-tetrahydroquinoline (**8b**)——Yellow prisms (from ether–hexane), mp 112—113°. IR ν_{max}^{Nujol} cm^{-1}: 1950, 1870, 1840 (C≡O), 1550 (Ar–N). NMR δ (d_6-acetone): 1.70—2.22 (2H, m), 2.51—2.86 (2H, m), 2.90 (3H, s, NCH_3), 3.06—3.36 (2H, m), 5.14 (1H, d, J=7.3 Hz, C_8–H), 5.82 (1H, dd, J=1.7 and 7.3 Hz, C_7–H), 5.96 (1H, d, J=1.7 Hz, C_5–H). *Anal.* Calcd for $C_{13}H_{12}ClCrNO_3$: C, 49.15; H, 3.81; Cl 11.16; N, 4.41. Found: C, 49.39; H, 3.83; Cl, 11.14; N, 4.21. [75% yield, **7b** (20%) was also recovered].

CTC-1-Benzyl-5-chloroindoline (**9a**)——Yellow crystals (from CH_2Cl_2–hexane), mp 123—124°. IR ν_{max}^{Nujol} cm^{-1}: 1960, 1894, 1883, 1850 (C≡O), 1552 (Ar–N). NMR δ (d_6-acetone): 2.70—3.52 (4H, m), 3.75 (1H, d, J=15.0 Hz, N–CH–Ph), 4.39 (1H, d, J=15.0 Hz, N–CH–Ph), 5.15 (1H, d, J=6.6 Hz, C_7–H), 5.71 (1H, dd, J=1.8 and 6.6 Hz, C_6–H), 5.99 (1H, d, J=1.8 Hz, C_4–H), 7.33 (5H, s, Ar–H of benzyl). *Anal.* Calcd for $C_{18}H_{14}ClCrNO_3$: C, 56.93; H, 3.71; Cl, 9.33; N, 3.69. Found: C, 56.75; H, 3.66; Cl, 9.30; N, 3.59. (92% yield).

CTC-1-Benzyl-6-chloro-1,2,3,4-tetrahydroquinoline (**9b**)——A yellow, viscous, unstable oil. After silica-gel chromatography, this was used directly for the next reaction. IR ν_{max}^{neat} cm^{-1}: 1960, 1870 (C≡O), 1545 (Ar–N). (91% yield).

CTC-5-Methoxy-1-methylindoline (**10a**)——Dry MeOH (0.145 ml, 4 equiv.) was carefully added to a suspension of potassium hydride (285 mg, 4 equiv.) in dry benzene (15 ml). 18-Crown-6 (117 mg, 0.5 equiv.) was then added and the mixture was heated at 75°. After 30 min, the CTC-complex **9a** (270 mg) was added all at once and the whole was stirred for 3 hr at 75°. The solution was worked up in the same way as for **8a** to give a yellow solid (228 mg, 85%), which was recrystallized from ether–hexane to give yellow needles of mp 61—62°. IR ν_{max}^{Nujol} cm^{-1}: 1930, 1853, 1830 (C≡O), 1560, 1530 (Ar–N and Ar–O). NMR δ (d_6-acetone): 2.52 (3H, s, NCH_3), 2.58—3.62 (4H, m), 3.68 (3H, s, OCH_3), 5.04—5.64 (3H, m, Ar–H). *Anal.* Calcd for $C_{13}H_{13}CrNO_4$: C, 52.18; H, 4.37; N, 4.68. Found: C, 52.31; H, 4.36; N, 4.41. The compounds **10b**, **11a**, and **11b** were prepared in the same way.

6-Methoxy-1-methyl-1,2,3,4-tetrahydroquinoline (**10b**)——Yellow prisms (from CH_2Cl_2–hexane), mp 118—119°. IR ν_{max}^{Nujol} cm^{-1}: 1935, 1920, 1845, 1820 (C≡O), 1565, 1530 (Ar–N and Ar–O). NMR δ (d_6-acetone): 1.80—2.20 (2H, m), 2.52—3.33 (4H, m), 2.79 (3H, s, NCH_3), 3.66 (3H, s, OCH_3), 5.11 (3H, m, Ar–H). *Anal.* Calcd for $C_{14}H_{15}CrNO_4$: C, 53.67; H, 4.82; N, 4.47. Found: C, 53.55; H, 4.78; N, 4.45. (85% yield).

CTC-1-Benzyl-5-methoxyindoline (**11a**)——Pale yellow needles (from CH_2Cl_2–hexane), mp 120—121°. IR ν_{max}^{Nujol} cm^{-1}: 1940, 1860 (C≡O), 1560, 1530 (Ar–N and Ar–O). NMR δ (d_6-acetone): 2.60—3.72 (5H, m), 3.66 (3H, s, OCH_3), 4.28 (1H, d, J=14.4 Hz, N–CH–Ph), 5.12—5.30 (2H, m, Ar–H), 5.51—5.68 (1H, m, Ar–H), 7.32 (5H, s, Ar–H of benzyl). *Anal.* Calcd for $C_{19}H_{17}CrNO_4$: C, 60.80; H, 4.56; N, 3.73. Found: C, 60.66; H, 4.51; N, 3.73. (92% yield).

CTC-1-Benzyl-6-methoxy-1,2,3,4-tetrahydroquinoline (**11b**)——A yellow, viscous oil (unstable). IR ν_{max}^{neat} cm^{-1}: 1950, 1860 (C≡O), 1560 (Ar–N and Ar–O). (91% yield).

5-Methoxy-1-methylindoline (**12a**)——CTC-Complex **10a** (155 mg) was dissolved in THF (5 ml) and, after the addition of 10%HCl (5 ml), iodine (520 mg) in THF (2 ml) was added dropwise. The mixture was stirred for 30 min at room temperature, then 20%$NaHSO_3$ solution was added until the solution turned

21) Commercially available potassium hydride showed 24—25% activity but the grey precipitates deposited on the bottom of the bottle showed *ca.* 40—45% activity.

green. The mixture was made alkaline with 20%NaOH and was then extracted with ether. The extract was dried over Na_2SO_4 and concentrated to afford a brown oil, which was chromatographed on alumina. Elution with CH_2Cl_2 gave 80 mg (95%) of a yellow oil (**12a**). IR ν_{max}^{neat} cm^{-1}: 1595 (Ar). NMR δ (d_6-acetone): 2.63 (3H, s, NCH_3), 3.66 (3H, s, OCH_3). MS *m/e*: 163 (M^+), 148 (M^+-Me). Picrate: yellow needles (from acetone), mp 170—171° (dec.). *Anal.* Calcd for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.10; N, 14.28. Found: C, 48.99; H, 4.17; N, 13.91. The compounds **12b** and **13a, b** were prepared in the same way.

6-Methoxy-1-methyl-1,2,3,4-tetrahydroquinoline (12b)——A yellow oil (99% yield). IR ν_{max}^{neat} cm^{-1}: 1610, 1577 (Ar). NMR δ ($CDCl_3$): 2.73 (2H, t, J=6.8 Hz), 2.80 (3H, s, NCH_3), 3.09 (2H, t, J=5.6 Hz), 3.69 (3H, s, OCH_3). MS *m/e*: 177 (M^+), 162 (M^+-Me). Picrate: yellow needles (from EtOH–$CHCl_3$), mp 146—147° (dec.). *Anal.* Calcd for $C_{17}H_{18}N_4O_8$: C, 50.25; H, 4.46; N, 13.78. Found: C, 49.95; H, 4.54; N, 13.39.

1-Benzyl-5-methoxyindoline (13a)——A pale yellow oil (90% yield). IR ν_{max}^{neat} cm^{-1}: 1596 (Ar). NMR δ ($CDCl_3$): 3.69 (3H, s, OCH_3), 4.13 (2H, s, N–CH_2–Ph), 6.38 (1H, d, J=8.5 Hz, C_7–H), 6.59 (1H, dd, J=2.4 and 8.5 Hz, C_6–H), 6.72 (1H, d, J=2.4 Hz, C_4–H). Hydrochloride: colorless prisms (from EtOH), mp 183—184° (dec.). *Anal.* Calcd for $C_{16}H_{18}ClNO$: C, 69.68; H, 6.57; Cl, 12.85; N, 5.07. Found: C, 69.48; H, 6.56; Cl, 12.92; N, 4.92.

1-Benzyl-6-methoxy-1,2,3,4-tetrahydroquinoline (13b)——A yellow oil (92% yield). IR ν_{max}^{neat} cm^{-1}: 1605, 1585 (Ar). NMR δ ($CDCl_3$): 1.95 (2H, quintet, J=6.0 Hz), 2.76 (2H, t, J=6.0 Hz), 3.23 (2H, t, J=6.0 Hz), 3.65 (3H, s, OCH_3), 4.36 (2H, s, N–CH_2–Ph), 7.22 (5H, s, Ar–H of benzyl). MS *m/e*: 253 (M^+), 162 (M^+-CH_2Ph). Hydrochloride: colorless prisms (from EtOH), mp 187—188° (dec.). *Anal.* Calcd for $C_{17}H_{20}ClNO$: C, 70.46; H, 6.94; Cl, 12.23; N, 4.83. Found: C, 70.05; H, 6.97; Cl, 12.32; N, 4.90.

Chlorination of 1,3,3-Trimethyloxindole (14) with NCS——1,3,3-Trimethyloxindole (**14**) (11.6 g) [prepared according to Julian's method[17]] was dissolved in 80%*tert*-BuOH (150 ml), and NCS (14.2 g) was added to this solution. The mixture was stirred for 17 hr at 50°, then allowed to come to room temperature, diluted with water, and extracted with ether. The extract was dried over Na_2SO_4 and concentrated to give a brown oil, which was triturated with hexane. Insoluble materials were removed by filtration. The filtrate was concentrated and the residue was subjected to silica-gel chromatography. Elution with EtOAc–benzene (1:2) afforded 9.62 g of 5-chloro-1,3,3-trimethyloxindole (**15**, 69%), together with 5,7-dichloro-1,3,3-trimethyloxindole (2.27 g, 15%). **15**: white prisms (from cyclohexane), mp 86—87°. IR ν_{max}^{Nujol} cm^{-1}: 1710 (C=O), 1620 (Ar). NMR δ (CCl_4): 1.32 (6H, s, >CMe_2), 3.15 (3H, s, NCH_3). MS *m/e*: 211 (M^++2), 209 (M^+), 194 (M^+-Me). *Anal.* Calcd for $C_{11}H_{12}ClNO$: C, 63.01; H, 5.76; Cl, 16.90; N, 6.68. Found: C, 62.90; H, 5.72; Cl, 17.05; N, 6.64. 5,7-Dichloro-1,3,3-trimethyloxindole: pale orange prisms (from cyclohexane), mp 114—115°. IR ν_{max}^{Nujol} cm^{-1}: 1720 (C=O), 1610, 1572 (Ar). NMR δ (CCl_4): 1.34 (6H, s, >CMe_2), 3.53 (3H, s, NCH_3), 6.96 (1H, d, J=2.0 Hz, C_4–H), 7.12 (1H, d, J=2.0 Hz, C_6–H). MS *m/e*: 247 (M^++4), 245 (M^++2), 243 (M^+), 228 (M^+-Me).

Chlorination of 3,3-Dimethyloxindole (16) with 1-Chlorobenzotriazole——3,3-Dimethyloxindole (**16**, 2.0 g) [prepared according to Julian's procedure[17]] was dissolved in dry CH_2Cl_2 (50 ml) and 1-chlorobenzotriazole (2.08 g) was added to this solution. The mixture was stirred for 17 hr at room temperature and concentrated to give a yellow oil, which was dissolved in EtOH (20 ml). Conc. HCl (3 ml) was added to this solution and the whole was stirred for 30 min at room temperature. The mixture was then concentrated and made alkaline by the addition of 20%NaOH. The mixture was extracted with ether and the extract was washed with 10%NaOH, dried over $MgSO_4$, and concentrated to give 2.2 g of 5-chloro-3,3-dimethyloxindole (91%) as a pale brown solid. Recrystallization from benzene gave colorless needles of mp 154—155°. IR ν_{max}^{Nujol} cm^{-1}: 1730, 1670 (C=O), 1620 (Ar). NMR δ ($CDCl_3$): 1.40 (6H, s, >CMe_2), 6.78—7.23 (3H, m, Ar–H), 9.65 (1H, br s, NH). *Anal.* Calcd for $C_{10}H_{10}ClNO$: C, 61.39; H, 5.14; Cl, 18.12; N, 7.15. Found: C, 61.48; H, 5.15; Cl, 18.12; N, 7.09.

5-Chloro-1,3,3-trimethyloxindole (15) by N-Methylation of 5-Chloro-3,3-dimethyloxindole——18-Crown-6 (200 mg) was added to a suspension of potassium hydride (1.1 g) in dry benzene under nitrogen. 5-Chloro-3,3-dimethyloxindole (1.5 g) in benzene (30 ml) was added dropwise to this solution at room temperature, and the mixture was stirred for 1 hr. Methyl iodide (0.95 ml) was added to this solution and the whole was stirred for another 2 hr. The mixture was then washed with brine, dried over $MgSO_4$, and concentrated to give a colorless oil and a solid. The solid was collected by filtration and washed with hexane to give 895 mg of **15**. The filtrate was concentrated and subjected to silica-gel chromatography with EtOAc–benzene (1:2) as an eluent to give 600 mg of **15** (total yield 93%), which was found to be identical with the product obtained by NCS chlorination of **14**.

5-Chloro-1,3,3-trimethylindoline (17)——Oxindole **15** (3.0 g) in dry ether (15 ml) was added dropwise to a suspension of $LiAlH_4$ (800 mg) in dry ether (30 ml) under ice cooling. The mixture was stirred for 2 hr at room temperature and then refluxed for another 2 hr. Water (0.8 ml), 15%NaOH (0.8 ml), and water (2.4 ml) were successively added to the reaction mixture under ice cooling. The resulting white precipitate was removed by filtration and the filtrate was dried over $MgSO_4$. The ether layer was concentrated to give a brown oil, which was chromatographed on silica-gel to give 2.42 g of a brown oil **17** (87%). IR ν_{max}^{neat} cm^{-1}: 1610 (Ar). NMR δ ($CDCl_3$): 1.28 (6H, s, >CMe_2), 2.70 (3H, s, NCH_3), 3.06 (2H, s, N–CH_2–C), 6.31 (1H, d, J=8.2 Hz, C_7–H). MS *m/e*: 197 (M^++2), 195 (M^+), 180 (M^+-Me). Picrate: yellow prisms (from EtOH), mp 144—145° (dec.). *Anal.* Calcd for $C_{17}H_{17}ClN_4O_7$: C, 48.06; H, 4.03; Cl, 8.34; N, 13.18. Found: C,

47.88; H, 4.01; Cl, 8.31; N, 12.74.

CTC-5-Chloro-1,3,3-trimethylindoline (18)——A mixture of indoline **17** (2.124 g), $Cr(CO)_6$ (7.1 g, 3 equiv.), diglyme (30 ml) and cyclohexane (30 ml) was heated under reflux (bath temp.: 125—130°) for 50 hr under an atmosphere of nitrogen. The mixture was cooled under nitrogen, then ether was added and the solution was successively washed with cold 10%HCl and water. The ether layer was dried over $MgSO_4$ and concentrated to give an orange oil, which was triturated with hexane. The resulting yellow solid was collected by filtration and washed with hexane to give 1.79 g of CTC-complex **18** (50% yield) as a yellow powder. Recrystallization from ether–hexane gave orange prisms of mp 132—133°. IR ν_{max}^{Nujol} cm^{-1}: 1950, 1850 (C≡O), 1555 (Ar–N). NMR δ (d_6-acetone): 1.32 (3H, s, –C(CH$_3$)–), 1.43 (3H, s, –C(CH$_3$)–), 2.69 (3H, s, NCH_3), 2.93 (1H, d, J=9.6 Hz, N–CH–C(–)), 3.26 (1H, d, J=9.6 Hz, N–CH–C(–)), 4.98 (1H, d, J=7.1 Hz, C_7–H), 5.90 (1H, dd, J=1.8 and 7.1 Hz, C_6–H), 6.08 (1H, d, J=1.8 Hz, C_4–H). *Anal.* Calcd for $C_{14}H_{14}ClCrNO_3$: C, 50.69; H, 4.25; Cl, 10.68; N, 4.22. Found: C, 50.80; H, 4.28; Cl, 10.51; N, 4.24.

CTC-5-Methoxy-1,3,3-trimethylindoline (19a)——CTC-Complex **18** was treated with "naked" methoxide anion in the manner described for **10a** (70°, 1 hr) and the resulting crude product was chromatographed on silica-gel with CH_2Cl_2–benzene (1: 3) as an eluent to afford **19a** as a yellow solid (93% yield). Recrystallization from ether–hexane gave yellow prisms of mp 90—91°. IR ν_{max}^{Nujol} cm^{-1}: 1940, 1850 (C≡O), 1560, 1530 (Ar–N and Ar–O). NMR δ (d_6-acetone): 1.29 (3H, s, –C(CH$_3$)–), 1.41 (3H, s, –C(CH$_3$)–), 2.59 (3H, s, NCH_3), 2.79 (1H, d, J=9.6 Hz, N–CH–C(–)), 3.19 (1H, d, J=9.6 Hz, N–CH–C(–)), 3.66 (3H, s, OCH_3), 4.95 (1H, d, J=7.1 Hz, C_7–H), 5.46 (1H, dd, J=1.8 and 7.1 Hz, C_6–H), 5.77 (1H, d, J=1.8 Hz, C_4–H). *Anal.* Calcd for $C_{15}H_{17}CrNO_4$: C, 55.04; H, 5.23; N, 4.27. Found: C, 54.89; H, 5.28; N, 4.27.

5-Methoxy-1,3,3-trimethylindoline (20a)——CTC-Complex **19a** was treated with iodine in the manner described for **12a** to give **20a** as a pale brown oil (96% yield). IR ν_{max}^{neat} cm^{-1}: 1600 (Ar). NMR δ ($CDCl_3$): 1.28 (6H, s, >C(CH$_3$)$_2$), 2.69 (3H, s, NCH_3), 3.05 (2H, s, N–CH$_2$–C(–)), 3.74 (3H, s, OCH_3). Picrate: yellow-green prisms (from EtOH), mp 153—154° (dec.). *Anal.* Calcd for $C_{18}H_{20}N_4O_8$: C, 51.43; H, 4.79; N, 13.32. Found: C, 51.29; H, 4.80; N, 13.32.

5-Benzyloxy-1,3,3-trimethylindoline (20b)——Benzyl alcohol (182 mg) was added slowly to a suspension of potassium hydride (170 mg) in dry benzene under nitrogen. 18-Crown-6 (111 mg) was then added to this solution and the whole was heated gradually to 75°. CTC-Complex **18** (140 mg) was added and the mixture was stirred for 30 min at 75°. The resulting solution was worked up as usual to give 160 mg (94%) of **19b** as a yellow viscous oil, which was treated with iodine in the manner described for **12a** to give a red oil (110 mg). The crude product was chromatographed on silica-gel to give 85 mg (80% yield) of **20b** as a white solid, which was recrystallized from hexane to give colorless scales of mp 60—61°. IR ν_{max}^{Nujol} cm^{-1}: 1595 (Ar). NMR δ ($CDCl_3$): 1.26 (6H, s, >C(CH$_3$)$_2$), 2.69 (3H, s, NCH_3), 3.01 (2H, s, N–CH$_2$–C(–)), 4.96 (2H, s, O–CH$_2$–Ph), 6.38 (1H, d, J=9.0 Hz, C_7–H), 6.70 (2H, m, C_4– and C_6–H), 7.34 (5H, m, Ar–H of benzyl). *Anal.* Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 81.02; H, 7.88; N, 5.15.

Acknowledgement The authors are grateful to Dr. Hiroshi Yamazaki of this Institute for valuable discussions. Financial support from the Ministry of Education, Science and Culture of Japan (Grant-in-Aid for Special Project Research) is gratefully acknowledged.