[Chem. Pharm. Bull. 29(3) 699—710 (1981)]

Fischer Indolization and Its Related Compounds. XV.[1] Vilsmeier-Haack Reaction of 1,2,3,4-Tetrahydrocarbazole Derivatives

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(Received September 22, 1980)

Treatment of 6-chloro-1,2,3,4-tetrahydrocarbazole (**14**) with the Vilsmeier-Haack reagent gave 6-chloro-2,3,4,4a-tetrahydrocarbazole-4a,9-dicarboxaldehyde (**16**) as a main product, along with 6-chloro-1,2,3,4-tetrahydrocarbazole-9-carboxaldehyde (**15**) and 6-chloro-1,2,3,4-tetrahydro-1-hydroxycarbazole-9-carboxaldehyde (**17**). The structures were established by spectral and chemical means. The mechanism of formation of **16** is discussed; in connection with this, a similar reaction of 6-chloro-1,2,3,4-tetrahydro-1,1-dimethylcarbazole (**37**) was carried out and found to yield three products, 6-chloro-1,2,3,4-tetrahydro-1,1-dimethylcarbazole-9-(**38**), 5-(**39**), and 7-carboxaldehyde (**40**).

Keywords——Vilsmeier-Haack reaction; 1,2,3,4-tetrahydrocarbazole; formylation; reactive center; structure; mechanism

In 1949, Pausacker *et al.*[3] reported the unexpected formation of 12-methoxy-1,2,3,4-tetrahydroisocarbazole (**1**) together with the normally expected 8-methoxy-1,2,3,4-tetrahydrocarbazole (**2**) in the Fischer indolization of cyclohexanone *o*-methoxyphenylhydrazone (**3**) in dilute sulfuric acid. In 1969, Gannon *et al.*[4] reexamined Pausacker's experiment and showed that the elemental analysis data for the unexpected product (**1**) were consistent with the empiri-

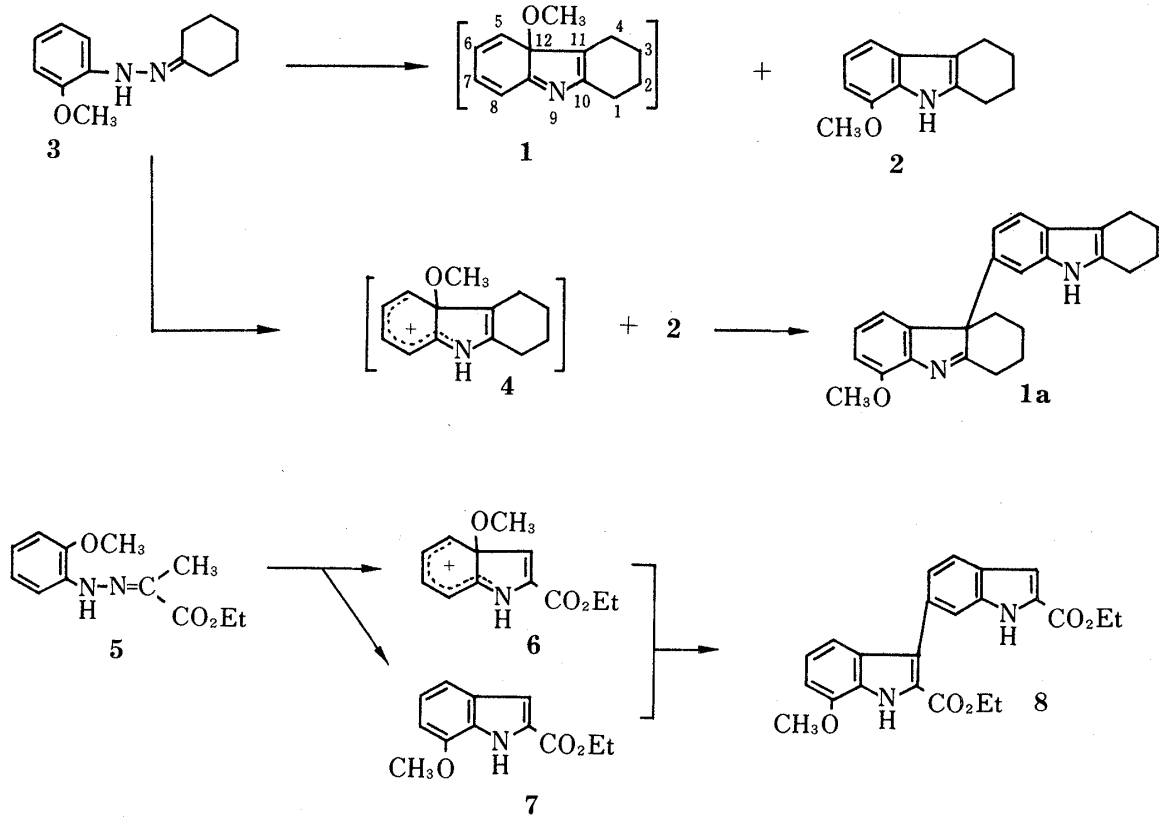

Chart 1

cal formula $C_{25}H_{26}N_2O$ and that it displayed a parent peak at *m/e* 370 in the mass spectrum. In the nuclear magnetic resonance (NMR) spectrum, it showed one NH, one methoxy, and six to seven aromatic protons in a complex system. On the other hand, during our studies on abnormal Fischer indolization, we[5] found that the *o*-methoxyphenylhydrozone derivative (**5**) cyclizes at the *ortho* position occupied by a methoxy group to give an intermediate cation (**6**). This cation (**6**) attacks the C_3-position of the expected indole product (**7**) in the reaction mixture to give a 3,6′-biindole (**8**). Thus, we proposed[5a] a new dimeric structure (**1a**) for Pausacker's compound (Chart 1). In order to clarify the presumed attack of the intermediate cation (**4**) on the 4a-position of 8-methoxy-1,2,3,4-tetrahydrocarbazole (**2**), chemical evidence regarding the behavior of 1,2,3,4-tetrahydrocarbazole (THC) with electrophilic reagents was desirable. In 1969, Yonemitsu *et al.*[6] reported that polyphosphate ester (PPE) attacked the C_4-position of THC (**9**) to give 4a-ethyl-1,2,3,4-tetrahydrocarbazolenine (**10**), whereas, in 1957, a Russian group[7] described the formation of N-formyl-THC (**11**) in 65% yield as a sole product in the Vilsmeier-Haack reaction[8] [V.-H. reaction] of THC (**9**) with diethylformamide and phosphorus oxychloride ($POCl_3$) as reagents. Since our results and Yonemitsu's report allude to the preferential attack of an electrophilic reagent on the 4a-position of THC (**9**) with respect to the nitrogen atom, we decided to reexamine the V.-H. reaction of THC (**9**).

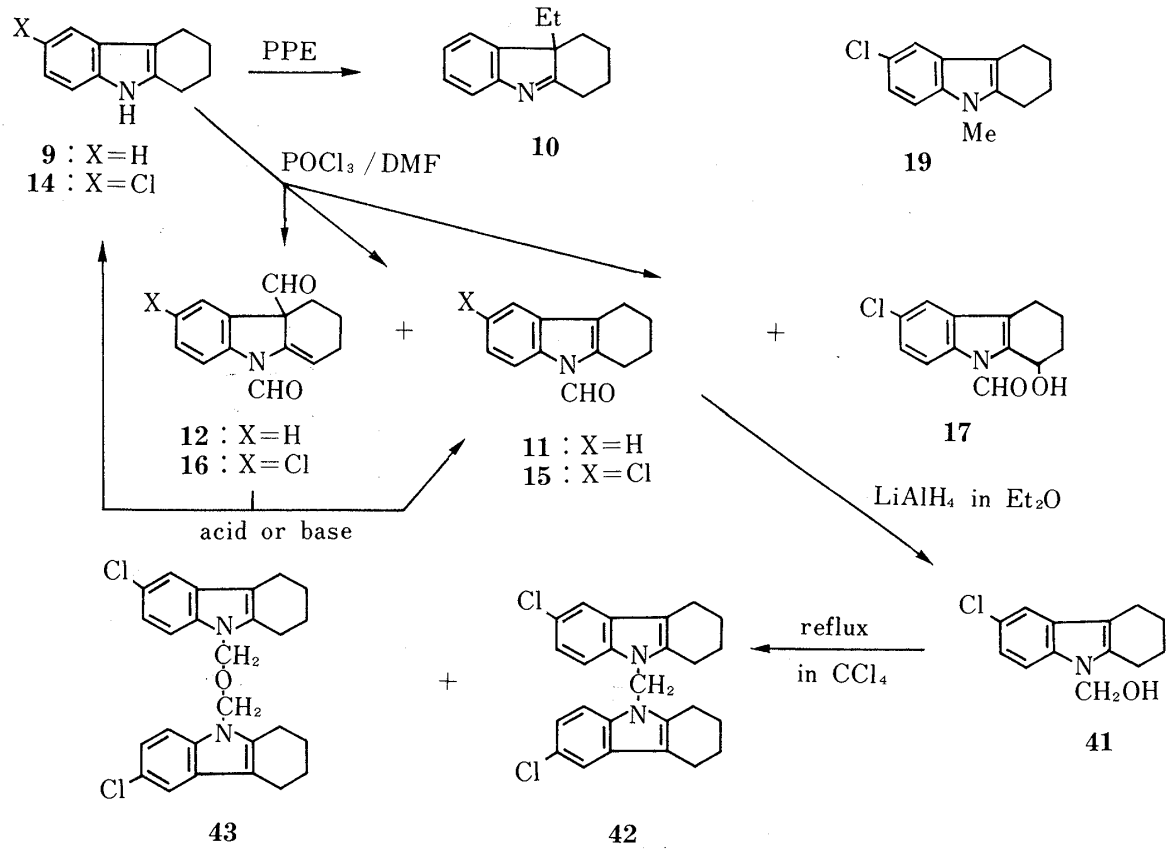

Chart 2

Treatment of THC (**9**) with dimethylformamide (DMF) and $POCl_3$ [V.-H. reagent] gave a mixture of N-formyl-THC (**11**) and an oily by-product (**12**) in 36.6% and 17.7% yields, respectively. In the mass spectrum, the by-product (**12**) shows the parent peak at *m/e* 227, corresponding to a molecular formula of $C_{14}H_{13}NO_2$. In its infrared (IR) spectrum, two carbonyl bands appear at 1725 and 1682 cm^{-1}. In the nuclear magnetic resonance (NMR) spectrum, it shows two 1H singlets due to formyl protons at 9.21 (sharp) and 8.84 δ (broad), and a 1H broad signal due to a vinylic proton. Chemically, treatment of this material (**12**)

with 2,4-dinitrophenylhydrazine gave a mono-2,4-dinitrophenylhydrazone derivative (**13**); this was confirmed by elemental analysis ($C_{20}H_{17}N_5O_5$). These results suggested that this compound could be a diformyl derivative, 2,3,4,4a-tetrahydrocarbazole-4a,9-dicarboxaldehyde (**12**). However, it was so labile that all attempts at further characterization failed, and therefore we changed the model substrate from THC (**9**) to 6-chloro-THC[9] (**14**), which gave a more stable by-product on similar treatment with the V.-H. reagent.

Treatment of 6-chloro-THC (**14**) with the V.-H. reagent afforded three products [Chart 2]. The first product (**15**), mp 145—147°, which was isolated in 1.5% yield, was established as N-formyl-6-chloro-THC (**15**) from its spectral data (see "Experimental"). It should be noted here that introduction of a chlorine atom at the C_6-position of the THC skeleton changed the N-formyl derivative from a major product to a very minor one.

The second product (the 6-chloro-diformyl derivative) (**16**), mp 134.5—136.5°, was obtained as a main product in 44.9% yield. Its molecular formula was confirmed to be $C_{14}H_{12}ClNO_2$ by elemental analysis and measurement of its mass spectrum. In the IR spectrum, it shows two carbonyl bands at 1720 and 1680 cm^{-1}. Furthermore, in the NMR spectrum, the presence of two formyl protons and one vinyl proton is indicated by the appearance of two 1H singlets at 8.98 (broad) and 9.61 δ (sharp), and a 1H broad signal at 5.94 δ. Treatment of the 6-chloro-diformyl derivative (**16**) with either boron trifluoride in acetic acid or an aqueous ethanol solution of sodium carbonate readily regenerated the starting 6-chloro-THC (**14**) with the N-formyl product (**15**). This means that no essential decomposition of the THC skeleton in this compound (**16**) took place during the V.-H. reaction. Although catalytic hydrogenation of the 6-chloro-diformyl derivative (**16**) on 5% palladium-carbon in ethanol or platinum oxide in acetic acid resulted in recovery of the starting material, treatment of it (**16**) with sodium borohydride gave an alcohol (**18**), $C_{14}H_{14}ClNO_2$, which shows hydroxy and carbonyl absorption at 3435 and 1665 cm^{-1}, respectively, in its IR spectrum. In the NMR spectrum, there are two doublets (each 1H, d, J=11.2 Hz) at 3.34 and 3.76 δ, indicating the presence of a tertiary hydroxymethyl group in the molecule. On the other hand, reduction of the 6-chloro-diformyl derivative (**16**) with lithium aluminum hydride gave N-methyl-6-chloro-THC (**19**), which was identical with an authentic sample prepared by N-methylation of the starting 6-chloro-THC (**14**) [Chart 3]. These results indicate that two formyl groups are present at both the nitrogen atom and the C_{4a}-angular position of the THC skeleton. The formation of N-methyl-

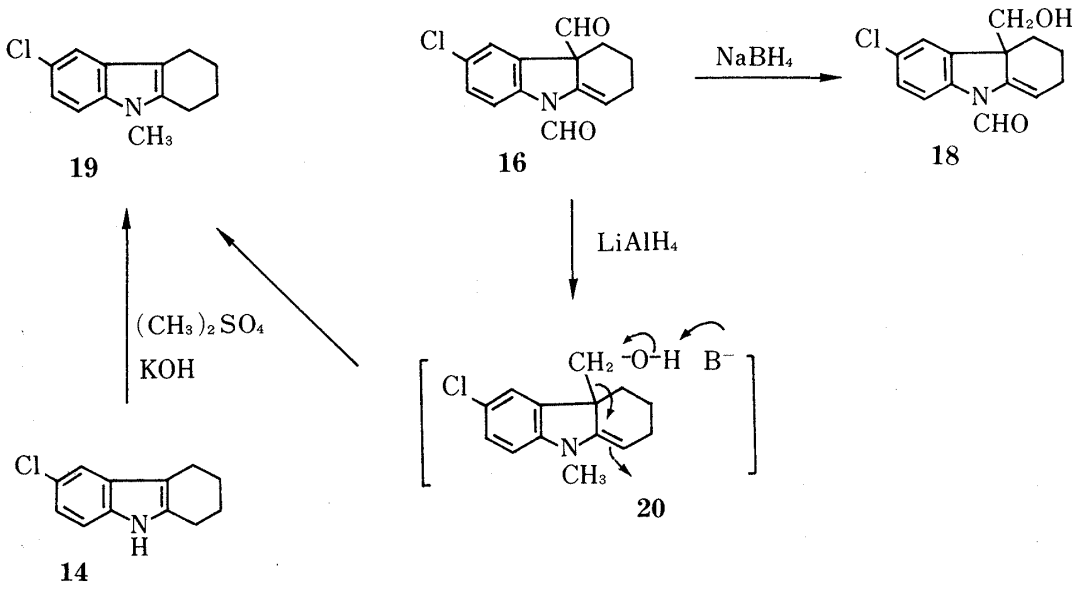

Chart 3

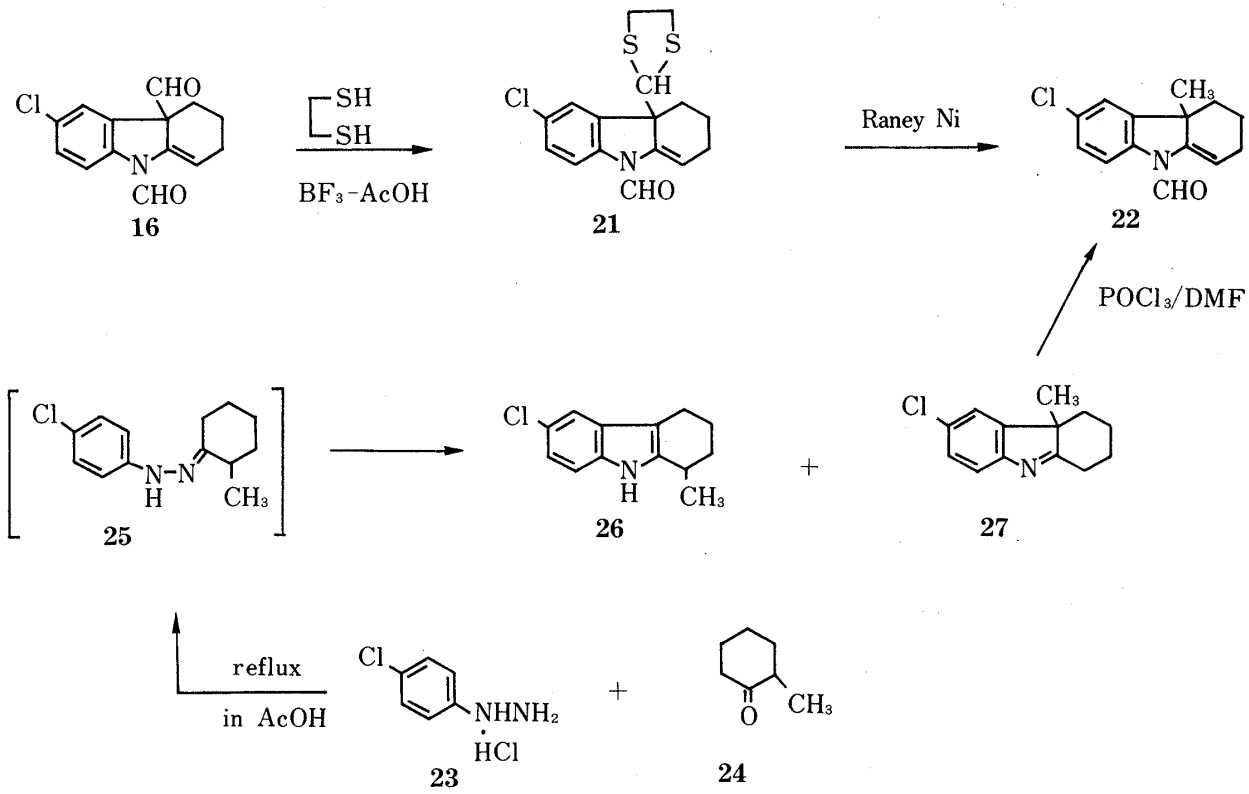

Chart 4

6-chloro-THC (**19**) in this reaction can be rationalized by supposing that the 4a-hydroxymethyl-N-methyl compound (**20**) was initially produced as an unstable intermediate and underwent deformylation by the attack of a base.

Treatment of the 6-chloro-diformyl derivative (**16**) with 1,2-ethanedithiol and boron trifluoride in acetic acid followed by desulfurization with Raney nickel gave a methyl-formyl derivative (**22**) [Chart 4]. On the other hand, a mixture of 4-chlorophenylhydrazine hydrochloride (**23**) and 2-methylcyclohexanone (**24**) was refluxed to give two products, mp 94—96° (**26**) and mp 80.5—81.5° (**27**), in 4% and 96% yields, respectively. Since both products (**26** and **27**) have the same molecular formula, $C_{13}H_{14}ClN$, these should be isomeric products formed by cyclization at each α-position of the phenylhydrazone (**25**). Since the ultraviolet (UV) spectrum of the minor product (**26**) is superimposable on that of 6-chloro-THC (**14**), as shown in Fig. 1, we can safely assign it as 1-methyl-6-chloro-THC (**26**). In other words, the major product should be the alternative one, the 4a-methylcarbazolenine (**27**). These assignments were supported by the fact that, in the NMR spectrum of the former compound (**26**), the signal due to a C-methyl group appeared as a doublet (J=7.3 Hz) at δ 1.28, but in that of the latter (**27**) it appeared as a singlet at δ 1.27. Treatment of the indolenine compound (**27**) with the V.-H. reagent provided

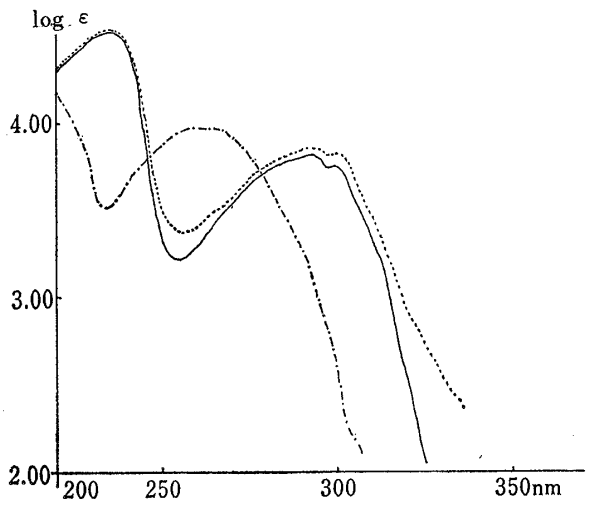

Fig. 1. The UV Spectra of **14**, **26**, and **27** in EtOH
——: **14**, ------: **26**, —·—: **27**.

the methyl-formyl derivative (**22**) which was identical with a specimen prepared from the diformyl derivative (**16**), indicating that the structure of the starting diformyl compound was 6-chloro-2,3,4,4a-tetrahydrocarbazole-4a,9-dicarboxaldehyde (**16**). This conclusion, moreover, is consistent with the formation of 2,3,4,4a-tetrahydrocarbazole-4a,9-dicarboxaldehyde (**12**) by a similar attack of the V.-H. reagent on a 4a-position in the case of THC (**9**) itself.

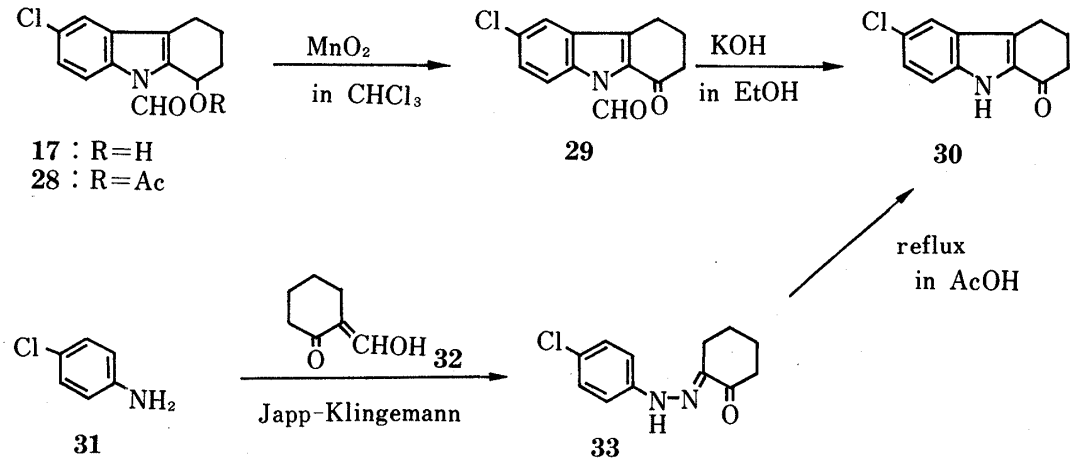

Chart 5

The third product (the hydroxy-amide) (**17**) was obtained as colorless pillars, mp 178—180.5°, in 14.8% yield [Chart 2]. Its molecular formula, $C_{13}H_{12}ClNO_2$, was confirmed by elemental analysis and mass spectroscopy. In the IR spectrum, it shows a hydroxy band at 3375 cm^{-1} and a carbonyl at 1675 cm^{-1}. Treatment of it with acetic anhydride in pyridine gave the acetoxy-amide (**28**), $C_{13}H_{11}ClNO_2$ (COMe), in 70.5% yield. In the IR spectrum, it shows an acetate band at 1728 cm^{-1} and an amide band at 1702 cm^{-1}, but no hydroxy or NH band. Oxidation of the hydroxy-amide (**17**) with active manganese dioxide in chloroform afforded the corresponding keto-amide (**29**), which shows no hydroxy band but has carbonyl bands at 1667 and 1697 cm^{-1} in the IR spectrum [Chart 5]. These results show that the hydroxy-amide (**17**) has an N-formyl group and a new allylic hydroxy group. Hydrolysis of the keto amide (**29**) with ethanolic potassium hydroxide afforded the NH-keto derivative (**30**). Since the characteristic feature of a 2-acylindole (λ_{max} 310.5 nm) was observed in the UV spectrum, it was supposed to be 6-chloro-3,4-dihydrocarbazole-1(2H)-one (**30**). The validity of this assumption was confirmed by an alternative synthesis of the NH-keto derivative (**30**) *via* Japp-Klingemann reaction[10] of *p*-chloroaniline (**31**) with 2-hydroxymethylenecyclohexanone[11] (**32**), followed by Fischer indolization.

On the formation of the diformyl derivative (**16**) from 6-chloro-THC (**14**), there are two possible reaction sequences, *i.e.*, with formylation at the nitrogen atom prior to the 4a-position and *vice versa* (Chart 6). In order to examine the former sequence (Chart 6; path A), we treated N-formyl-6-chloro-THC (**15**) with the V.-H. reagent under the conditions used in the experiment on 6-chloro-THC (**14**). The actual reaction species is, of course, different from N-formyl-6-chloro-THC (**15**) at the stage of second formylation of an N-attacked product but the complex (**34**). Since we[12] had experienced an exchange of the acyl group during the V.-H. reaction of various amide derivatives, N-formyl-6-chloro-THC (**15**) was expected to be present as the complex (**34**) when treated with the V.-H. reagent. The trial resulted in the recovery of the starting material (**15**). This result left it unclear whether N-formyl-6-chloro-THC (**15**) is a product of the V.-H. reaction of 6-chloro-THC (**14**) or an artefact formed by hydrolysis of the diformyl derivative (**16**) during work-up, because treatment of the diformyl derivative (**16**)

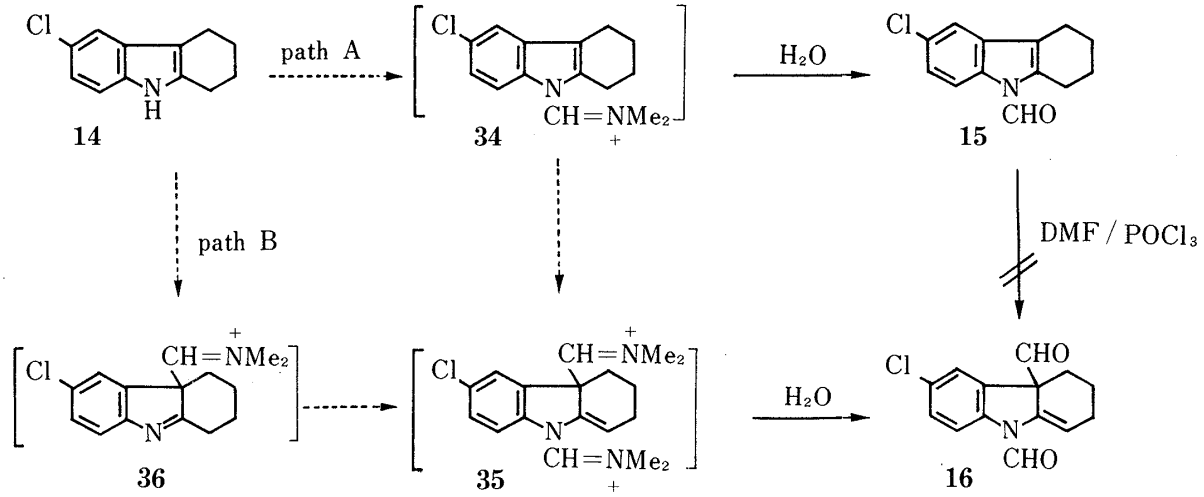

Chart 6

under acidic or basic conditions gave a mixture of the starting material (**14**) and N-formyl-6-chloro-THC (**15**) [Chart 2].

Thus, we examined the V.-H. reaction of 1,1-dimethyl-6-chloro-THC (**37**), in which the second formylation was forbidden by the presence of a *gem*-dimethyl group at the C_1-position. When 1,1-dimethyl-6-chloro-THC (**37**) was treated with the V.-H. reagent under slightly more severe conditions, three products (**38**, **39**, and **40**) were produced in 8.9%, 5.0%, and 59.8% yields, respectively. Since these three products have the same molecular formula, $C_{15}H_{16}ClNO$, and each of them shows a carbonyl band in the IR spectrum and a 1H aldehydic signal in the NMR spectrum, we may conclude that each product is formylated at a different position of the starting material (**37**) [Chart 7].

The first compound (**38**) shows no NH band in the IR spectrum and has three aromatic protons in its NMR spectrum. These results determine its structure as the N-formyl derivative (**38**).

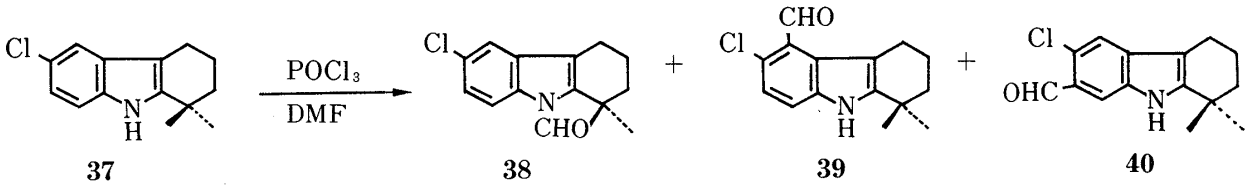

Chart 7

The second compound (**39**) shows NH bands at 3237 and 3207 cm^{-1} in the IR spectrum. Furthermore, in the NMR spectrum, it shows only two 1H doublets (J=8.8 Hz) coupled to each other in the aromatic region. Thus ,it may be assigned as the 5-formyl derivative (**39**).

The third (**40**), the main product, also shows an NH band at 3342 cm^{-1} in its IR spectrum. However, in the NMR spectrum, its two aromatic protons appear as singlets at 7.38 and 7.80 δ. From these data, we decided this product was formylated at the benzene moiety, *i.e.*, it was the 7-formyl derivative (**40**).

This result shows clearly that the presence of a *gem*-dimethyl group at the C_1-position sterically hindered both N- and C_{4a}-formylation. Unfortunately, we could not obtain positive evidence for electrophilic attack at the C_{4a}-position of the THC skeleton prior to the nitrogen atom in the formation of the 6-chloro-diformyl derivative (**16**). However, it seems reasonable to assume that the complex (**36**) is a transient intermediate leading to the diformyl derivative (**16**), because, as shown above, the 4a-methylcarbazolenine (**27**) smoothly gave the methyl-

formyl derivative (**22**) in the V.-H. reaction in good yield under even milder conditions than 6-chloro-THC (**14**) itself did (Chart 4).

Finally, some interesting results were obtained during attempts to transform N-formyl-6-chloro-THC (**15**) to N-methyl-6-chloro-THC (**19**) [Chart 2]. Treatment of N-formyl-6-chloro-THC (**15**) with lithium aluminum hydride unexpectedly gave the N-hydroxymethyl derivative (**41**), which is so labile that it decomposed gradually even during measurement of the NMR spectrum in carbon tetrachloride solution at room temperature. The molecular formula of this material (**41**) was found to be $C_{13}H_{14}ClNO$ by elemental analysis and measurement of the mass spectrum. In the IR spectrum, it shows a hydroxy band at 3360 cm^{-1} and the presence of an NCH_2O group in its molecule was confirmed by the appearance of a 2H sharp singlet at 5.27 δ in its NMR spectrum. This finding is consistent with the documented observation[13] that N-acylindole derivatives form the corresponding 2,4-dinitrophenylhydrazones, indicating that N-acylindole derivatives show some ketonic character.

It is also interesting that, when refluxed in carbon tetrachloride, the N-hydroxymethyl derivative (**41**) provided two dimeric products (**42**: mp 267 —269° and **43**: mp 142.5—144.5°) in 15.6% and 59.3% yields. The molecular formulae of the products were found to be $C_{25}H_{24}Cl_2N_2$ (the parent peak at *m/e* 422) (**42**) and $C_{26}H_{26}Cl_2N_2O$ (the parent peak at *m/e* 452) (**43**), respectively, by elemental analysis and mass spectroscopy. Although, unfortunately, their NMR spectrum could not be measured because of their insolubility in various solvents, their structures were supposed to be the dimeric N-methylene (**42**) and the dimeric ether (**43**) shown in Chart 2. It is not difficult to understand the formation of these products in carbon tetrachloride if the presence of a trace amount of hydrogen chloride in the solution is assumed.

Experimental

All melting points were measured on a micro melting point hot stage (Yanagimoto) and are uncorrected. IR, NMR and mass spectra were obtained with Hitachi EPI-G3, JEOL JMN-4H-100, and Hitachi RMU-6E spectrometers, respectively. In the NMR spectrum, chemical shifts are given in δ-values referred to internal tetramethylsilane, and the assignment of all NH and OH signals were confirmed by the disappearance of their signals after addition of D_2O. Mass spectra were measured by the direct inlet system. For chromatography (by column), silicic acid (SiO_2), 100 mesh, Mallinckrodt Chemical Works and for preparative TLC, Kiesel gel GF_{254}, Merck, were used. Identification of the products was done by IR, mixed melting point determination, and TLC. The abbreviations used are as follows: s, singlet; d, doublet; d.d, double doublet; t, triplet; q, quartet; m, multiplet; dif, diffused; sh, shoulder.

General Procedure for the Vilsmeier-Haack Reaction of 1,2,3,4-Tetrahydrocarbazole Derivatives——A 1,2,3,4-tetrahydrocarbazole derivative was added to an ice-cooled solution of $POCl_3$ in dry DMF. The mixture was heated at 70—80° (bath temperature) for 20 min, poured into ice-water, basified with 10% Na_2CO_3 aq., and extracted with Et_2O. The ethereal layer was washed with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residue was chromatographed on SiO_2 with an appropriate solvent.

Vilsmeier-Haack Reaction of THC [1,2,3,4-Tetrahydrocarbazole] (**9**)——THC[14] (**9**) (1.00 g) was treated according to the general procedure with $POCl_3$ (0.895 g) and DMF (14 ml). The reaction product (1.149 g) was chromatographed on SiO_2 with benzene as a solvent.

N-Formyl-THC [1,2,3,4-Tetrahydrocarbazole-9-carboxaldehyde][7] (**11**)——The first elution gave colorless prisms (0.426 g), mp 64—65°, which were recrystallized from hexane. *Anal.* Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.07; H, 6.55; N, 6.94. IR ν_{max}^{Nujol} cm^{-1}: NH (nil), 1694 (C=O). NMR (CCl_4) δ: 1.87 (4H, m, C_2– and C_3–H), 2.55 (2H, m, C_4–H), 2.80 (2H, m, C_1–H), 7.15 (3H, m, C_5–, C_6– and C_7–H), 8.15 (1H, br, $W_{1/2}$=18.5 Hz, C_8–H), 9.01 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 247 (4.29), 252.5 sh (4.25), 268 sh (3.99), 303 (3.61). MS *m/e*: 199 (M^+).

The Diformyl Derivative [2,3,4,4a-Tetrahydrocarbazole-4a,9-dicarboxaldehyde] (**12**)——The second elution gave an oily product (0.235 g) as a labile compound. IR ν_{max}^{liquid} cm^{-1}: NH (nil), 1725, 1682 (C=O). NMR (CCl_4) δ: 1.40—3.00 (6H, m, C_2–, C_3– and C_4–H), 5.63 (1H, br.s, C_1–H), 7.04—7.50 (3H, m, C_5–, C_6–, and C_7–H), 7.98 (1H, br.d, J=7.3 Hz, C_8–H), 8.84 (1H, br.s, NCHO), 9.21 (1H, s, C–CHO). UV λ_{max}^{EtOH} nm: 242, 270, 295 sh. MS *m/e*: 227 (M^+, $C_{14}H_{13}NO_2$). 2,4-Dinitrophenylhydrazone (**13**): A solution of the diformyl derivative (**12**) (70 mg) in EtOH (1 ml) was added to a cold solution of 2,4-dinitrophenylhydrazine (80 mg) in sulfuric acid (conc. H_2SO_4, 0.4 ml; H_2O, 0.6 ml). Precipitates were collected by filtration and washed with EtOH. Recrystallization from dioxane–H_2O gave yellow fine needles (80 mg), mp 234—235°. *Anal.* Calcd for $C_{20}H_{17}N_5O_5$: C, 58.96; H, 4.21; N, 17.19. Found: C, 58.95; H, 4.05; N, 17.11. IR ν_{max}^{Nujol}

cm^{-1}: 3275 (NH), 1680 (C=O). MS *m/e*: 407 (M^+).

Vilsmeier-Haack Reaction of 6-Chloro-THC [6-Chloro-1,2,3,4-tetrahydrocarbazole] (14)——The general procedure was carried out on 6-chloro-THC (**14**) (4.12 g) with $POCl_3$ (9.20 g) and dry DMF (60 ml). The reaction mixture was chromatographed on SiO_2 with benzene as a solvent.

N-Formyl-6-chloro-THC [6-Chloro-1,2,3,4-tetrahydrocarbazole-9-carboxaldehyde] (15)——The first elution gave colorless prisms (72 mg), mp 145—147°, which were recrystallized from benzene–cyclohexane. *Anal.* Calcd for $C_{13}H_{12}ClNO$: C, 66.81; H, 5.18; N, 5.99. Found: C, 66.90; H, 5.14; N, 5.94. IR ν_{max}^{Nujol} cm^{-1}: NH (nil), 1695 (C=O). NMR ($CDCl_3$) δ: 1.90 (4H, m, C_2– and C_3–H), 2.60 (2H, m, C_4–H), 2.85 (2H, m, C_1–H), 7.22 (1H, d.d, J=2.5 and 8.5 Hz, C_7–H), 7.33 (1H, d, J=2.5 Hz, C_5–H), 8.20 (1H, br.d, J=8.5 Hz, C_8–H), 9.07 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 250 (4.34), 274 sh (3.99), 282 sh (3.92), 300 (3.63), 309 (3.58). MS *m/e*: 235 (M^++2, 34.4% of the intensity of M^+), 233 (M^+).

The 6-Chloro-diformyl Derivative [6-Chloro-2,3,4,4a-tetrahydrocarbazole-4a,9-dicarboxaldehyde] (16)——The second elution gave colorless cubes (2.353 g), mp 134.5—136.5°, which were recrystallized from benzene–cyclohexane. *Anal.* Calcd for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.35; H, 4.54; N, 5.37. IR ν_{max}^{Nujol} cm^{-1}: 1720 and 1680 (C=O). NMR (DMSO-d_6) δ: 1.30—2.90 (6H, m, aliphatic H), 5.94 (1H, br.s, C_1–H), 7.36 (1H, d.d, J=2.0 and 8.5 Hz, C_7–H), 7.49 (1H, d, J=2.0 Hz, C_5–H), 7.90 (1H, br.d, J=8.5 Hz, C_8–H), 8.98 (1H, br.s, NCHO), 9.61 (1H, s, C–CHO). UV λ_{max}^{EtOH} nm (log ε): 247 (3.93), 273 (4.01), 302 sh (3.54). MS *m/e*: 263 (M^++2, 36.6% of the intensity of M^+), 261 (M^+).

The Hydroxy-amide [6-Chloro-1,2,3,4-tetrahydro-1-hydroxycarbazole-9-carboxaldehyde] (17)——The third elution with $CHCl_3$ gave colorless pillars (0.737 g), mp 178—180.5°, which were recrystallized from EtOH–benzene–cyclohexane. *Anal.* Calcd for $C_{13}H_{12}ClNO_2$: C, 62.53; H, 4.84; N, 5.61. Found: C, 62.49; H, 4.92; N, 5.37. IR ν_{max}^{Nujol} cm^{-1}: 3375 (OH), 1675 (C=O). NMR ($CDCl_3$) δ: 1.50—2.80 (7H, m, C_2–, C_3–, and C_4–H, and OH), 5.05 (1H, dif.s, C_1–H), 7.20—7.45 (2H, m, C_5– and C_7–H), 7.50—8.30 (1H, br. signal, C_8–H), 9.33 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 248.5 (4.42), 272.5 sh (4.07), 279.5 sh (4.00), 299 (3.79), 308.5 (3.75). MS *m/e*: 251 (M^++2, 34.8% of the intensity of M^+), 249 (M^+).

Treatment of the 6-Chloro-diformyl Derivative (16) with BF_3–Et_2O——A mixture of the 6-chloro-diformyl derivative (**16**) (100 mg) and BF_3–Et_2O (0.1 ml) in AcOH (1.5 ml) was refluxed for 30 min, then poured into water and extracted with Et_2O. The ethereal layer was washed with 5% $NaHCO_3$ aq. and water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residue (78 mg) was chromatographed on SiO_2 with benzene as a solvent. The first elution gave 6-chloro-THC (**14**) (22 mg), mp 149—151.5°, which was identified by comparison with an authentic sample. The second elution gave N-formyl-6-chloro-THC (**15**) (40 mg), mp 143.5—147°, which was identified by comparison with an authentic sample.

Treatment of the 6-Chloro-diformyl Derivative (16) with Na_2CO_3 aq. in EtOH——An aqueous solution of Na_2CO_3 [82 mg in water (1 ml)] was added to a solution of the 6-chloro-diformyl derivative (**16**) (100 mg) in EtOH (4 ml). The resulting suspension was stirred for 6 hr at room temperature, then poured into water, and extracted with Et_2O. The ethereal layer was washed with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Preparative TLC of the residue (91 mg) gave N-formyl-6-chloro-THF (**15**) (11 mg) and the starting material (**16**) (33 mg). The presence of 6-chloro-THC (**14**) in the reaction mixture was observed on a TLC plate but it could not be isolated because of the small quantity formed.

The Alcohol [6-Chloro-2,3,4,4a-tetrahydro-4a-hydroxymethylcarbazole-9-carboxaldehyde] (18)——$NaBH_4$ (100 mg) was added portionwise to a suspension of the 6-chloro-diformyl derivative (**16**) (200 mg) in EtOH (5 ml) during 15 min under cooling with a freezing mixture (ice-NaCl). After being stirred for a further 1 hr, the reaction mixture was poured into cold water and extracted with Et_2O. The ethereal layer was washed with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Column chromatography of the residue (224 mg) on SiO_2 with benzene–ethyl acetate (8: 2) as a solvent gave colorless fine needles (175 mg), mp 162.5—164°, which were recrystallized from benzene. *Anal.* Calcd for $C_{14}H_{14}ClNO_2$: C, 63.76; H, 5.35; N, 5.31. Found: C, 63.74; H, 5.32; N, 5.28. IR ν_{max}^{Nujol} cm^{-1}: 3435 (OH), 1666 (C=O). NMR ($CDCl_3$) δ: 1.30—2.60 (6H, m, C_2–, C_3–, and C_4–H), 1.73 (1H, br.s, OH), 3.45 and 3.76 (each 1H, d, J=11.2 Hz, $-C\underline{H}_2OH$), 5.55 (1H, br.s, $W_{1/2}$=10.7 Hz, C_1–H), 7.10—7.37 (2H, m, C_5– and C_7–H), 8.00 (1H, br.s, $W_{1/2}$=17.0 Hz, C_8–H), 8.78 (1H, br.s, CHO). UV λ_{max}^{EtOH} nm (log ε): 247.5 (3.93), 272.5 (4.02), 302.5 sh (3.57). MS *m/e*: 265 (M^++2, 34.6% of the intensity of M^+), 263 (M^+).

Reduction of the 6-Chloro-diformyl Derivative (16) with $LiAlH_4$ [Formation of N-Methyl-6-chloro-THC (19)]——The diformyl derivative (**16**) (200 mg) was added to a suspension of $LiAlH_4$ (250 mg) in dry Et_2O (20 ml) under ice-cooling and the mixture was refluxed for 2.5 hr. The reaction complex was decomposed by addition of 3% NaOH aq. (1 ml) under ice-cooling. The precipitates were filtered off and washed with Et_2O. The filtrate and the washings were combined, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Column chromatography of the residue (174 mg) on SiO_2 with benzene as a solvent gave colorless leaflets (121 mg), mp 53—54°, which were recrystallized from EtOH–H_2O. This material was identical with an authentic sample of N-methyl-6-chloro-THC (**19**) which was prepared by N-methylation of 6-chloro-THC (**14**).

N-Methyl-6-Cl-THC [6-Chloro-1,2,3,4-tetrahydro-9-methylcarbazole[15]] (19)——Dimethyl sulfate (6.00 g) was added to a stirred solution of 6-chloro-THC (**14**) (4.00 g) in acetone (50 ml) containing 50% KOH aq. (16 ml). The mixture was stirred for 2.5 hr at room temperature, poured into water, and extracted with

Et_2O. The ethereal layer was dried over anhydrous K_2CO_3 and evaporated to dryness *in vacuo*. The residue was dissolved in acetone (50 ml) containing 50% KOH aq. (8 ml) and treated with dimethyl sulfate (3.00 g) again. The reaction mixture (6.752 g) was dissolved in benzene and chromatographed on SiO_2 to give colorless leaflets (4.25 g), mp 53—55° (lit.[15] mp 53—54°), which were recrystallized from EtOH or aqueous EtOH. *Anal.* Calcd for $C_{13}H_{14}ClN$: C, 71.06; H, 6.42; N, 6.38. Found: C, 70.86; H, 6.35; N, 6.36. IR ν_{max}^{Nujol} cm^{-1}: no characteristic band. NMR (CCl_4) δ: 1.87 (4H, m, C_2– and C_3–H), 2.65 (4H, m, C_1– and C_4–H), 3.53 (3H, s, NMe), 6.95 (2H, dif.s, C_7– and C_8–H), 7.27 (1H, dif.s, C_5–H). UV λ_{max}^{EtOH} nm (log ε): 238.5 (4.56), 287 sh (3.73), 295 (3.78), 303 sh (3.74). MS *m/e*: 221 (M^++2, 32.6% of the intensity of M^+), 219 (M^+).

The Dithioacetal [6-Chloro-4a-ethylenedithiomethyl-2,3,4,4a-tetrahydrocarbazole-9-carboxaldehyde] (21)——BF_3–Et_2O (0.1 ml) was added to a suspension of the 6-chloro-diformyl derivative (**16**) (100 mg) and 1,2-ethanedithiol (0.1 ml) in AcOH (1 ml) at room temperature. The mixture was allowed to stand for 2 hr at room temperature, poured into water, and extracted with Et_2O. The ethereal layer was washed with 5% $NaHCO_3$ aq., dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Column chromatography of the oily residue (163 mg) on SiO_2 with $CHCl_3$ as a solvent gave colorless fine prisms (53 mg), mp 148—150°, which were recrystallized from EtOH. *Anal.* Calcd for $C_{16}H_{16}ClNOS_2$: C, 56.87; H, 4.77; N, 4.15. Found: C, 56.60; H, 4.66; N, 3.90. IR ν_{max}^{Nujol} cm^{-1}: 1675 (C=O). NMR (CCl_4) δ: 1.60—2.48 (6H, m, C_2–, C_3–, and C_4–H), 2.70—3.10 (4H, m, SCH_2CH_2S), 4.92 (1H, s, $CH\langle^{S}_{S}$), 5.46 (1H, br.m, C_1–H), 7.22 (1H, d.d, J=2.0 and 8.5 Hz, C_7–H), 7.41 (1H, d, J=2.0 Hz, C_5–H), 7.99 (1H, d, J=8.5 Hz, C_8–H), 8.70 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 250 (3.97), 270 (3.98), 275 (3.98). MS *m/e*: 339 (M^++2, 40% of the intensity of M^+), 337 (M^+).

The Methyl-formyl Derivative [6-Chloro-2,3,4,4a-tetrahydro-4a-methylcarbazole-9-carboxaldehyde] (22)——Raney nickel[16] [prepared from alloy (8 g)] was added to a solution of the dithioacetal (**21**) (200 mg) in acetone (20 ml). The mixture was refluxed for 30 min and the nickel catalyst was filtered off. The catalyst was washed with acetone. The filtrate and washings were combined and evaporated to dryness *in vacuo*. The oily residue (132 mg) was chromatographed on SiO_2 with benzene as a solvent to give colorless leaflets (84 mg), mp 72.5—74.5°, which were recrystallized from aqueous EtOH. This material was identical with an authentic sample prepared by an alternative route.

An Alternative Synthesis of the Methyl-formyl Derivative (22)——2-Methylcyclohexanone (**24**) (2.24 g) was added to a solution of *p*-chlorophenylhydrazine·HCl (**23**) (3.58 g) in AcOH (20 ml) at room temperature. The mixture was refluxed for 15 min, poured into ice-water, basified with Na_2CO_3 aq., and extracted with Et_2O. The ethereal layer was washed with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The oily residue (4.932 g) was chromatographed on SiO_2 with benzene as a solvent.

a) 1-Methyl-6-chloro-THC [6-Chloro-1,2,3,4-tetrahydro-1-methylcarbazole] (**26**): The first elution gave an oil, which solidified gradually. Recrystallization of the crude crystalline material from aqueous EtOH gave colorless prisms (175 mg), mp 94—96°. *Anal.* Calcd for $C_{13}H_{14}ClN$: C, 71.06; H, 6.42; N, 6.38. Found: C, 71.19; H, 6.32; N, 6.21. IR ν_{max}^{Nujol} cm^{-1}: 3413 (NH). NMR (CCl_4) δ: 1.28 (3H, d, J=7.3 Hz, C_1–Me), 1.40—3.10 (7H, m, C_1–, C_2–, C_3–, and C_4–H), 6.95 (2H, m, C_6– and C_7–H), 7.27 (1H, dif.s, C_5–H), 7.45 (1H, br.s, NH). UV λ_{max}^{EtOH} nm (log ε): 234.5 (4.53), 284 (3.81), 292 (3.86), 300.5 (3.82). MS *m/e*: 221 (M^++2, 34.1% of the intensity of M^+), 219 (M^+).

b) The 4a-Methylcarbazolenine [6-Chloro-2,3,4,4a-tetrahydro-4a-methyl-1H-carbazole] (**27**): The second elution gave colorless needles (4.225 g), mp 80.5—81.5°, which were recrystallized from hexane. *Anal.* Calcd for $C_{13}H_{14}ClN$: C, 71.06; H, 6.42; N, 6.38; Cl, 16.14. Found: C, 71.19; H, 6.48; N, 6.14; Cl, 16.08. IR ν_{max}^{Nujol} cm^{-1}: NH (nil), 1580 (C=N). NMR (CCl_4) δ: 0.95—2.95 (8H, m, C_1–, C_2–, C_3– and C_4–H), 1.27 (3H, s, C–Me), 7.15 (1H, d, J=2.5 Hz, C_5–H), 7.21 (1H, d.d, J=2.5 and 9.0 Hz, C_7–H), 7.42 (1H, d, J=9.0 Hz, C_8–H). UV λ_{max}^{EtOH} nm (log ε): 262 (3.97). MS *m/e*: 221 (M^++2, 32.6% of the intensity of M^+), 219 (M^+).

c) Authentic Methyl-formyl Derivative [6-Chloro-2,3,4,4a-tetrahydro-4a-methylcarbazole-9-carboxaldehyde] (**22**): The 4a-methylcarbazolenine (**27**) (300 mg) was treated with $POCl_3$ (420 mg) in dry DMF (4 ml),[17] and worked-up according to the general method. Column chromatography of the reaction product (345 mg) on SiO_2 with benzene as a solvent gave colorless prisms (337 mg), mp 73—74.5°, which were recrystallized from aqueous EtOH. *Anal.* Calcd for $C_{14}H_{14}ClNO$: C, 67.88; H, 5.70; N, 5.65. Found: C, 67.87; H, 5.64; N, 5.57. IR ν_{max}^{Nujol} cm^{-1}: 1674 (C=O). NMR (CCl_4) δ: 1.27 (3H, s, C–Me), 1.40—2.40 (6H, m, C_2–, C_3–, and C_4–H), 5.35 (1H, br.s, C_1–H), 7.03 (1H, d, J=2.5 Hz, C_5–H), 7.15 (1H, d.d, J=2.5 and 9.0 Hz, C_7–H), 7.95 (1H, br. signal, C_8–H), 8.76 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 246 (3.93), 269 (4.01), 300 sh (3.60). MS *m/e*: 249 (M^++2, 32.9% of the intensity of M^+), 247 (M^+).

The Acetoxy-amide [6-Chloro-1,2,3,4-tetrahydro-1-acetoxycarbazole-9-carboxaldehyde] (28)——Acetic anhydride (0.5 ml) was added to a solution of the hydroxy-amide (**17**) (130 mg) in pyridine (2 ml). The mixed solution was allowed to stand overnight at room temperature, then poured into water, and extracted with Et_2O. The ethereal layer was washed with dil. HCl aq. and water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residue (129 mg) was chromatographed on SiO_2 with benzene as a solvent to give colorless needles (107 mg), mp 166—168°, which were recrystallized from benzene–cyclohexane. *Anal.* Calcd for $C_{15}H_{14}ClNO_3$: C, 61.75; H, 4.84; N, 4.80. Found: C, 61.87; H, 4.75; N, 4.76. IR ν_{max}^{Nujol} cm^{-1}: 1728

(OAc), 1702 (CHO). NMR (CCl_4) δ: 1.77—3.00 (6H, m, C_2–, C_3–, and C_4–H), 2.04 (3H, s, COMe), 6.19 (1H, br.m, $W_{1/2}$=6.4 Hz, C_1–H), 7.26 (1H, d.d, J=2.0 and 8.8 Hz, C_7–H), 7.36 (1H, d, J=2.0 Hz, C_5–H), 8.18 (1H, d, J=8.8 Hz, C_8–H), 9.03 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 248.5 (4.39), 275 sh (4.02), 299 (3.75), 308.5 (3.75). MS *m/e*: 293 (M^++2, 37.3% of the intensity of M^+), 291 (M^+).

The Keto-amide [6-Chloro-3,4-dihydro-1(2H)-oxo-carbazole-9-carboxaldehyde] (29)——Active MnO_2[18] (570 mg) was added to a solution of the hydroxy-amide (**17**) (112 mg) in $CHCl_3$ (7 ml). The suspension was stirred for 50 min at room temperature. The catalyst was filtered off and washed thoroughly with $CHCl_3$. The filtrate and washings were combined and evaporated to dryness *in vacuo*. Column chromatography of the residue (83 mg) on SiO_2 with benzene as a solvent gave colorless rods (59 mg), mp 185.5—186.5°, which were recrystallized from cyclohexane–benzene. *Anal.* Calcd for $C_{13}H_{10}ClNO_2$: C, 63.04; H, 4.07; N, 5.66. Found: C, 63.19; H, 4.03; N, 5.65. IR ν_{max}^{Nujol} cm^{-1}: 1697 (CHO), 1669 (C=O). NMR (DMSO-d_6) δ: 2.00—3.10 (6H, m, C_2–, C_3– and C_4–H), 7.59 (1H, d.d, J=2.0 and 8.8 Hz, C_7–H), 7.92 (1H, d, J=2.0 Hz, C_5–H), 8.33 (1H, d, J=8.8 Hz, C_8–H), 9.99 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 248.5 (4.23), 303 (4.30). MS *m/e*: 249 (M^++2, 32.7% of the intensity of M^+), 247 (M^+).

The NH-Keto Derivative [6-Chloro-3,4-dihydrocarbazole-1(2H)-one[19]] (30)——The crude keto-amide (**29**) (60 mg) was added to 50% KOH aq. (0.5 ml). The mixture was refluxed for 5 min, then poured into water, and extracted with Et_2O. The ethereal layer was washed with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Column chromatography of the residue (58 mg) on SiO_2 with 5% AcOEt in benzene as a solvent gave colorless needles (53 mg), mp 232—233°, which were recrystallized from benzene. *Anal.* Calcd for $C_{12}H_{10}ClNO$: C, 65.61; H, 4.59; N, 6.38. Found: C, 65.87; H, 4.54; N, 6.33. IR ν_{max}^{Nujol} cm^{-1}: 3260 (NH), 1640 (C=O). NMR (DMSO-d_6) δ: 2.00—3.05 (6H, m, C_2–, C_3– and C_4–H), 7.25 (1H, d.d, J=2.0 and 8.5 Hz, C_7–H), 7.42 (1H, d, J=8.5 Hz, C_8–H), 7.70 (1H, d, J=2.0, C_5–H), 11.75 (1H, br.s, NH). UV λ_{max}^{EtOH} nm (log ε): 238 (4.29), 310.5 (4.34). MS *m/e*: 221 (M^++2, 36% of the intensity of M^+), 219 (M^+). This material was identical with an authentic sample prepared *via* an alternative route.

Alternative Synthesis of the NH-Keto Derivative (30)——a) (Z)-1,2-Cyclohexanedione Mono(*p*-chlorophenylhydrazone)[19,20] (**33**): A solution of the diazonium salt prepared from *p*-chloroaniline (**31**) (6.75 g), $NaNO_2$ (3.70 g), conc. HCl (10.6 g), and water (30 ml) was added dropwise to a solution of 2-hydroxymethylenecyclohexanone[11] (**32**) (6.75 g) and 50% KOH aq. (KOH: H_2O=3 g: 3 ml) in EtOH (80 ml) under ice-cooling. The mixture was stirred for 30 min at room temperature, and poured into water. The precipitates were collected by filtration and recrystallized from benzene–EtOH to give yellow leaflets (11.48 g), mp 172—175° [lit.,[19] mp 163—164°]. *Anal.* Calcd for $C_{12}H_{13}ClN_2O$: C, 60.89; H, 5.54; N, 11.84. Found: C, 60.88; H, 5.46; N, 11.86. IR ν_{max}^{Nujol} cm^{-1}: 3231 (NH), 1662 (C=O). NMR ($CDCl_3$) δ: 1.70—2.00 (4H, m, aliphatic H), 2.35—2.60 (2H, m, aliphatic H), 2.60—2.85 (2H, m, aliphatic H), 7.07—7.33 (4H, m, aromatic H), 13.70 (1H, br.s, NH, disappeared on addition of D_2O). MS *m/e*: 238 (M^++2, 32.8% of the intensity of M^+), 236 (M^+).

b) The NH–Keto Derivative (**30**): A suspension of 1,2-cyclohexanedione mono(*p*-chlorophenylhydrazone) (**33**) (5.00 g) in AcOH (50 ml) was gently refluxed for 45 min, poured into water, and extracted with Et_2O. The ethereal layer was washed with 5% $NaHCO_3$ aq. and water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Column chromatography of the residue (4.50 g) on SiO_2 with $CHCl_3$ as a solvent gave colorless needles (1.356 g), mp 232—233.5° (lit.[19] mp 218—219°), which were recrystallized from benzene. *Anal.* Calcd for $C_{12}H_{10}ClNO$: C, 65.61; H, 4.59; N, 6.38. Found: C, 65.75; H, 4.49; N, 6.33.

1,1-Dimethyl-6-chloro-THC [6-Chloro-1,2,3,4-tetrahydro-1,1-dimethylcarbazole] (37)——2,2-Dimethyl cyclohexanone[21] (1.27 g) was added to a suspension of *p*-chlorophenylhydrazine·HCl (**23**) (1.80 g) in AcOH (10 ml). The mixture was gently refluxed for 20 min, then poured into water, and extracted with Et_2O. The ethereal solution was washed with dil. $NaHCO_3$ aq. and water, dried over anhydrous K_2CO_3, and evaporated to dryness *in vacuo*. Column chromatography of the residue (2.26 g) on SiO_2 with benzene–cyclohexane (2: 1) as a solvent gave colorless needles (1.135 g), mp 77.5—79.5°, which were recrystallized from hexane. *Anal.* Calcd for $C_{14}H_{16}ClN$: C, 71.94; H, 6.90; N, 5.99. Found: C, 71.98; H, 6.87; N, 5.88. IR ν_{max}^{Nujol} cm^{-1}: 3432 (NH). NMR (CCl_4) δ: 1.31 (6H, m, 2×Me), 1.60—2.00 (4H, m, C_2– and C_3–H), 2.50—2.70 (2H, m, C_4–H), 6.87—7.10 (2H, m, C_7– and C_8–H), 7.29 (1H, dif. s, C_5–H), 7.50 (1H, br.s, NH). UV λ_{max}^{EtOH} nm (log ε): 235 (4.56), 285 sh (3.80), 292 (3.84), 301 (3.78). MS *m/e*: 235 (M^++2, 37.5% of the intensity of M^+), 233 (M^+).

Vilsmeier-Haack Reaction of 1,1-Dimethyl-6-chloro-THC (37)——The general method was carried out on the 1,1-dimethyl-6-chloro-THC (**37**) (1.00 g) with $POCl_3$ (3.93 g) and DMF (12 ml) at 100—110° for 1.5 hr. The reaction mixture (1.031 g) was chromatographed on SiO_2 with benzene as a solvent.

The N-Formyl Product [6-Chloro-1,2,3,4-tetrahydro-1,1-dimethylcarbazole-9-carboxaldehyde] (38)——The first elution gave colorless needles (100 mg), mp 156.5—157.5°, which were recrystallized from hexane. *Anal.* Calcd for $C_{15}H_{16}ClNO$: C, 68.83; H, 6.16; N, 5.35. Found: C, 68.81; H, 6.03; N, 5.19. IR ν_{max}^{Nujol} cm^{-1}: NH (nil), 1691 (C=O). NMR (CCl_4) δ: 1.48 (6H, s, 2×Me), 1.70—2.00 (4H, m, C_2– and C_3–H), 2.47—2.65 (2H, m, C_4–H), 7.18 (1H, d.d, J=2.5 and 8.3 Hz, C_7–H), 7.25 (1H, d, J=2.5 Hz, C_5–H), 8.21 (1H, d, J=8.3 Hz, C_8–H), 9.40 (1H, s, CHO). UV λ_{max}^{EtOH} nm (log ε): 250.5 (4.35), 273 sh (4.02), 281 sh (3.96), 299 (3.64), 308.5 (3.58). MS *m/e*: 263 (M^++2, 35.5% of the intensity of M^+), 261 (M^+).

The 5-Formyl Product [6-Chloro-1,2,3,4-tetrahydro-1,1-dimethylcarbazole-5-carboxaldehyde] (39)——

The second elution gave pale yellow needles (57 mg), mp 233.5—235.5°, which were recrystallized from benzene. *Anal.* Calcd for $C_{15}H_{16}ClNO$: C, 68.83; H, 6.16; N, 5.35. Found: C, 68.80; H, 6.08; N, 5.54. IR ν_{max}^{Nujol} cm^{-1}: 3237, 3207 (NH), 1668 (C=O). NMR (DMSO-d_6) δ: 1.33 (6H, s, 2×Me), 1.50—1.90 (4H, m, C_2– and C_3–H), 2.60—2.85 (2H, m, C_4–H), 7.06 (1H, d, J=8.8 Hz, C_7– or C_8–H), 7.50 (1H, d, J=8.8 Hz, C_7– or C_8–H), 10.58 (1H, s, CHO), 11.26 (1H, br.s, NH). UV λ_{max}^{EtOH} nm (log ε): 256 (4.29), 358 (3.76), 376 (3.76). MS *m/e*: 263 (M^++2, 38% of the intensity of M^+), 261 (M^+).

The 7-Formyl Product [6-Chloro-1,2,3,4-tetrahydro-1,1-dimethylcarbazole-7-carboxaldehyde] (40)——The third elution gave pale yellow leaflets (669 mg), mp 255—255.5°, which were recrystallized from benzene. *Anal.* Calcd for $C_{15}H_{16}ClNO$: C, 68.83; H, 6.16; N, 5.35. Found: C, 68.90; H, 6.21; N, 5.31. IR ν_{max}^{Nujol} cm^{-1}: 3342 (NH), 1667 (C=O). NMR (DMSO-d_6) δ: 1.34 (6H, s, 2×Me), 1.60—2.00 (4H, m, C_2– and C_3–H), 2.60 (2H, m, C_4–H), 7.38 (1H, s, C_5– or C_8–H), 7.80 (1H, s, C_5– or C_8–H), 10.35 (1H, s, CHO), 11.27 (1H, br.s, NH). UV λ_{max}^{EtOH} nm (log ε): 245 (4.27), 268 (4.17), 328.5 (4.12), 375 (4.01). MS *m/e*: 263 (M^++2, 33.4% of the intensity of M^+), 261 (M^+).

The N-Hydroxymethyl Derivative [6-Chloro-1,2,3,4-tetrahydrocarbazole-9-methanol] (41)——N-Formyl-6-chloro-THC (**15**) (200 mg) was added to a suspension of $LiAlH_4$ (200 mg) in anhyd. Et_2O (15 ml) and the mixture was refluxed for 1.5 hr. The complex was decomposed by addition of 3% NaOH aq. (1 ml) under ice-cooling, then the precipitates were filtered off and washed with Et_2O. The combined filtrate and washings were dried over $MgSO_4$ and evaporated to dryness *in vacuo*. Column chromatography of the residue (196 mg) on SiO_2 with benzene as a solvent gave colorless prisms (133 mg), mp 103—104.5°, which were recrystallized from cyclohexane. *Anal.* Calcd for $C_{13}H_{14}ClNO$: C, 66.24; H, 5.99; N, 5.94. Found: C, 66.07; H, 5.90; N, 5.93. IR ν_{max}^{Nujol} cm^{-1}: 3360 (OH), C=O (nil). NMR (CCl_4) δ: 1.85 (4H, m, C_2– and C_3–H), 2.61 (4H, m, C_1– and C_4–H), 5.27 (3H, dif.s, NCH_2O and OH), 6.90—7.10 (2H, m, C_7– and C_8–H), 7.30 (1H, m, C_5–H). UV λ_{max}^{EtOH} nm (log ε): 236 (4.53), 285 sh (3.81), 291 (3.84), 301.5 sh (3.70). MS *m/e*: 237 (M^++2, 31% of the intensity of M^+), 235 (M^+).

Dimerization of the N-Hydroxymethyl Derivative (41)——A solution of the N-hydroxymethyl derivative (**41**) (100 mg) in CCl_4 was refluxed for 1.5 hr and then evaporated to dryness. Column chromatography of the residue (100 mg) on SiO_2 with benzene–cyclohexane (1:2) was carried out.

The Dimeric N-Methylene Compound [9,9′-Methylene Bis(6-Chloro-1,2,3,4-tetrahydrocarbazole)] (42)——The first elution gave colorless needles (14 mg), mp 267—269°, which were recrystallized from EtOH–$CHCl_3$. *Anal.* Calcd for $C_{25}H_{24}Cl_2N_2$: C, 70.92; H, 5.71; N, 6.62. Found: C, 71.16; H, 5.67; N, 6.49. IR ν_{max}^{Nujol} cm^{-1}: no characteristic band. UV λ_{max}^{EtOH} nm (log ε): 234.5 (4.77), 240 sh (4.72), 284 (4.09), 291 (4.10), 301 (3.98). MS *m/e*: 424 (M^++2, 70.6% of the intensity of M^+), 422 (M^+).

The Dimeric Ether {Bis[(6-Chloro-1,2,3,4-tetrahydrocarbazole-9-)methyl] Ether} (43)——The second elution gave colorless pillars (57 mg), mp 142.5—144.5°, which were recrystallized from cyclohexane. *Anal.* Calcd for $C_{26}H_{26}Cl_2N_2O$: C, 68.87; H, 5.78; N, 6.18. Found: C, 68.87; H, 5.93; N, 5.82. IR ν_{max}^{Nujol} cm^{-1}: no characteristic band. NMR (CCl_4) δ: 1.80 (8H, br.s, 2×C_2– and 2×C_3–H), 2.20—2.77 (8H, m, 2×C_1– and 2×C_4–H), 5.21 (4H, s, 2×–CH_2O), 6.92 (4H, m, 2×C_7– and 2×C_8–H), 7.31 (2H, d, J=1.3 Hz, 2×C_5–H). UV λ_{max}^{EtOH} nm (log ε): 235.5 (4.86), 285 sh (4.14), 293 (4.17), 302 (4.07). MS *m/e*: 454 (M^++2, 67.2% of the intensity of M^+), 452 (M^+).

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