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THE VILSMEIER-HAACK REACTION ON METHYL HOMOLOGUES OF *N*-BENZYLTETRAHYDROCARBAZOLE (SYNTHETIC STUDIES ON INDOLES 52[1]).

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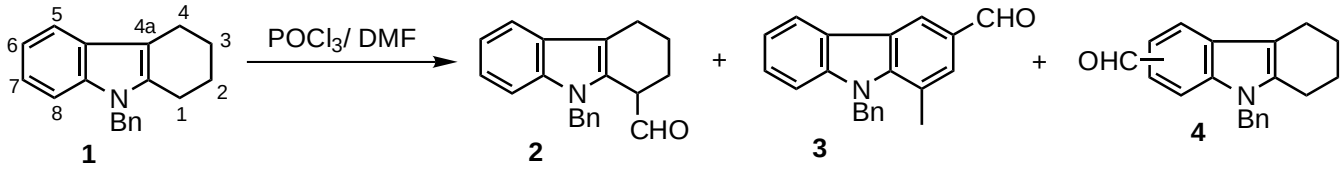
Abstract-To examine the steric effect in the Vilsmeier-Haack reaction of *N*-benzyl-1,2,3,4-tetrahydrocarbazole (**1**), the reactions were carried out on three methyl homologues of **1**. It was found that 1-methyl- or 4,4-dimethyl group has a large effect on reactivity due to their steric bulkiness. This result shows the importance of an initial attack at the 4a-position for the formation of these products.

We found[2,3] that the Vilsmeier-Haack (V-H) reaction of *N*-benzyl-1,2,3,4-tetrahydrocarbazole (BnTHC) (**1**) gave the formylated compounds (**2**, **3**, and **4**) which were formed to all appearances by the attack of the reagent at usually non or less reactive aliphatic position (Scheme 1). The proposed mechanism shows that the reagent initially attacked the 4a-position, followed by 1-position, except benzene-part formylated compounds (**4**). However, there was no evidence for an initial 4a-attack. In the previous paper[3] we examined the effect of reagents in order to examine the reactivity at the 4a-position by changing the size of reagents.



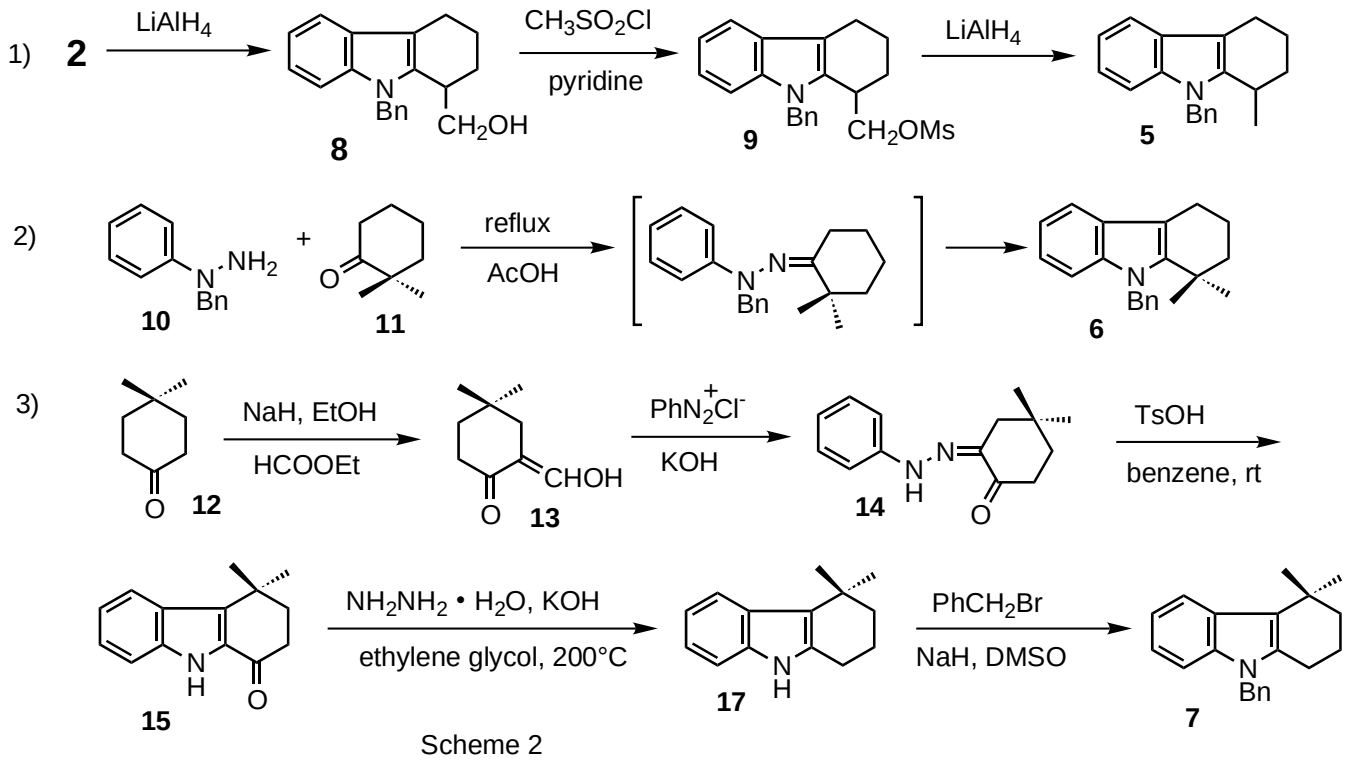
1 **2** **3** **4**

Scheme 1

In the present papers we report the V-H reaction of 1-methyl (**5**), 1,1-dimethyl (**6**)-, and 4,4-dimethyl (**7**) derivatives of BnTHC (**1**), in order to examine the steric effect in the substrates toward the 1- and 4-position. The V-H reaction of 4-methyl-BnTHC was already reported.[2] In this case product distribution was almost the same as that of BnTHC (**1**).

Preparation of methyl homologues of BnTHC (1), 5, 6, and 7

Unknown methyl homologues of BnTHC (**5**, **6**, and **7**) were prepared as shown in Scheme 2.



Scheme 2

The 1-methyl-BnTHC (**5**) was prepared starting from known 1-formyl-BnTHC (**2**). The compound (**2**) was reduced with $LiAlH_4$ to alcohol (**8**). After mesylation of **8**, the compound (**9**) was reduced with $LiAlH_4$ to give the desired compound (**5**).

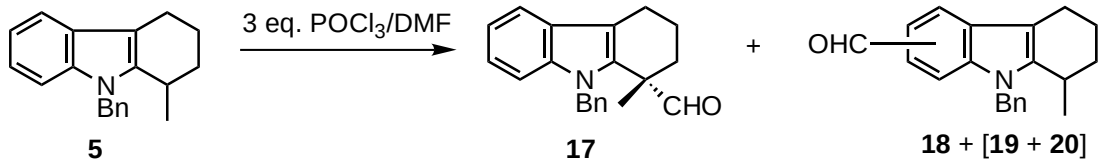
The 1,1-dimethyl-BnTHC (**6**) was simply prepared from 1-benzylphenylhydrazine (**10**) and 2,2-dimethylcyclohexanone [4] (**11**) under the condition of Fischer indole synthesis.

The 4,4-dimethyl-BnTHC (**7**) was prepared *via* Japp-Klingemann reaction. 4,4-Dimethylcyclohexanone[5] (**12**) was converted into 2-hydroxymethylene derivative[6] (corresponding 2-formyl derivative) (**13**), which was treated with the diazonium salt prepared from aniline under basic condition to give the phenylhydrazone (**14**). Treatment of **14** with TsOH in benzene (Fischer indole synthesis) gave 1-oxo-4,4-dimethyltetrahydrocarbazole (**15**). Huang-Minlon reduction of **15**, followed by *N*-benzylation gave the desired 4,4-dimethyl-BnTHC (**7**).

Vilsmeier-Haack formylation of the methyl homologues of BnTHC (1), 5, 6, and 7.

V-H formylation of **5**, **6**, and **7** was carried out with $POCl_3$ (3 mol eq.) in DMF at lower temperature (0 and/or 40°C) and higher temperature (120°C) according to the reference. [2] The products were isolated by column-chromatography, but 6- and 7-formyl compounds were generally hard to separate. They were identified as a mixture or a part of them were separated by liquid chromatography for characterization.

1) The V-H reaction of 1-methyl-BnTHC (**5**) gave the result shown in Scheme 3.



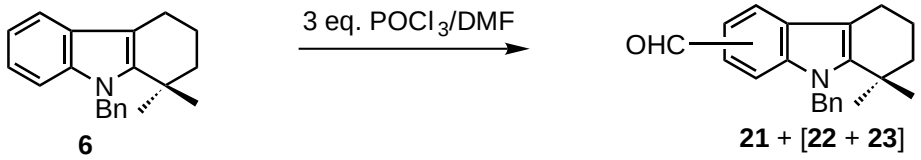
5 **17** **18** + [**19** + **20**]

Condition		Yield (%)	
temp./ time	**17**	**18**	**19** + **20**
0℃/ 72 h	83	1	10
120℃/ 30 min	13	5	64

Scheme 3

At 0°C, the 1-formyl product (**17**) was the main product, whereas at 120°C, the benzene-part formylated products (**18**, **19**, and **20**) prevailed. This result suggested that **17** was a kinetically controlled product, while the benzene-part formylated products (**18**, **19**, **20**) were thermodynamically controlled products.

2) The reaction of 1,1-dimethyl-BnTHC (**6**) gave the result shown in Scheme 4.



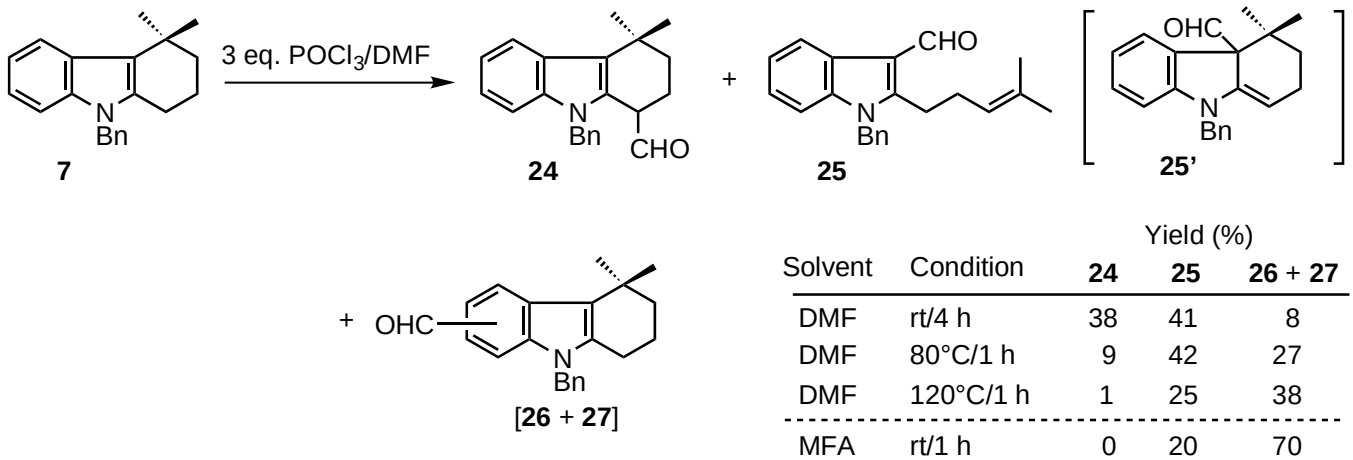
6 **21** + [**22** + **23**]

condition	Yield (%)		
temp./time	**21**	**22** + **23**	SM (**6**)
0°C/6.5 h	0.3	1	86
40°C/8 h	1.3	44	52
120°C/2 h	5	90	0

Scheme 4

In this case, there was no reaction occurring at the aliphatic portion. It is natural that products would only be benzene-part formylated products, as the substrate (**6**) has a dimethyl group at 1-position.

3) The reaction of 4,4-dimethyl-BnTHC (**7**) gave the result shown in Scheme 5.



7 **24** **25** **25'**

Solvent	Condition	Yield (%) **24**	**25**	**26** + **27**
DMF	rt/4 h	38	41	8
DMF	80°C/1 h	9	42	27
DMF	120°C/1 h	1	25	38
MFA	rt/1 h	0	20	70
MFA	120°C/1 h	0	0	89

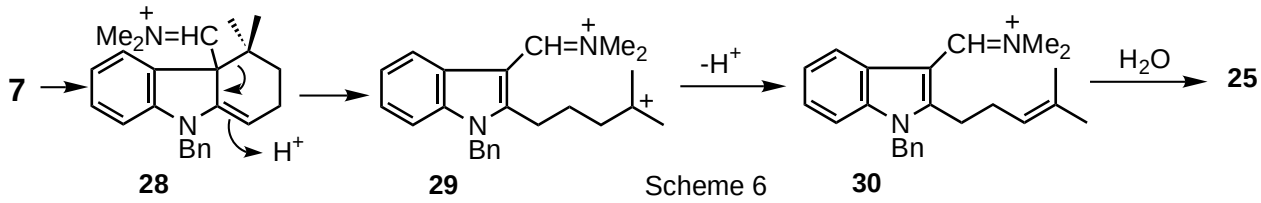
MFA: N-methylformanilide

Scheme 5

The yield of 1-formyl product (**24**) decreased with elevating temperature, whereas the yield of benzene-

part formylated products (**26** + **27**) increased. In this reaction, the ring-opened products (**25**) were newly formed. The yield of **25** slightly decreased with elevating temperature (Scheme 3). The reaction in *N*-methylformanilide which forms sterically more hindered reagent than DMF, was tried to examine the above inclination. In this reaction, there was no 1-formyl product (**24**) formed at all and the yield of the ring-opened product (**25**) decreased, while the yield of benzene-part formylated products (**26**, and **27**) increased with elevating temperature.

A possible mechanism of the formation of ring-opened product (**25**) is shown in Scheme 6.



Scheme 6

4,4-Dimethyl-Bn-THC (**7**) was attacked by V-H reagent at 4a-position to give **28**, which has a very crowded position at 4a. This steric stress broke the C4-C4a bond of **28** to give the ring-opened carbocation intermediate (**29**). The formation of this tertially cation would facilitate breaking of the C4-C4a bond. The intermediate (**29**) thus formed was converted to **25**.

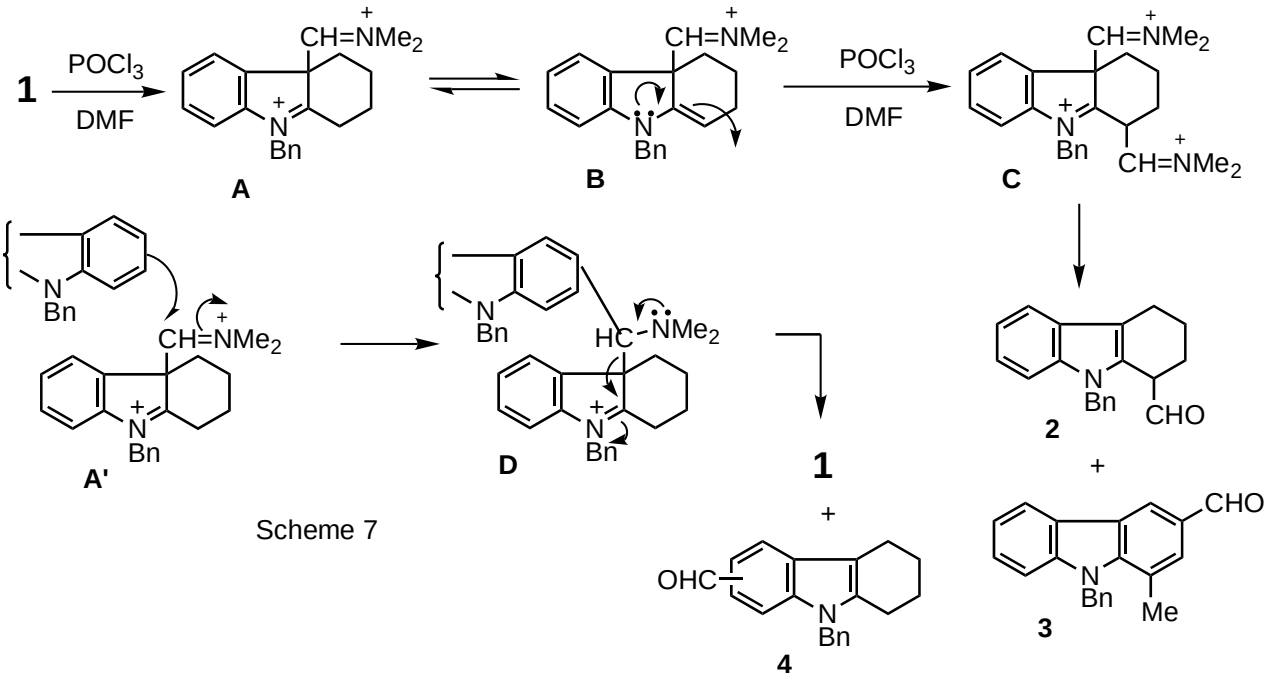
Structure determination of the products

The structure of the products obtained from methyl homologues of BnTHC (**1**), **5**, **6**, and **7**, resembled those obtained from BnTHC (**1**),[2] except the ring-opened product (**25**). Thus, the structures of the product except **25** were easily determined by elemental analysis and spectral data in comparison with those of the products from **1**. The benzene-formylated products were separated by chromatography, but some of them were separated only as a mixture of isomers . They were assigned as a single compound or as a mixture of isomers by ^{1}H-NMR and MS to be the formyl products. Although their ^{1}H-NMR spectra resembled those of the products obtained from BnTHC (**1**)[2)], the positions of the formyl group were not determined precisely, because they were not necessary for the present discussion. The position of the formyl group is shown as x, y, and z in **EXPERIMENTAL**. Compound (**25**) was a strange product in the V-H reaction of indoles. Initially, we supposed that the structure of **25** would be **25'**. However, after determination by spectral data, the structure of **25** was finally confirmed by X-Ray analysis as the semicarbazone.

Discussion

In the reactions of 1-methyl (**5**)- and 4,4-dimethyl (**7**)-BnTHC, the yields of 1-formyl products (**17** and **24**) were high, whereas the yields of benzene-part formylated product (**18**-**20** and **26**-**27**), were low, at a lower temperature. On the contrary, the yields of two kinds of products (**17**, **24**), and (**18**-**20**), (**26**-**27**) reversed at a higher temperature. It seemed strange that the most reactive position changed with temperature. This leads us to suppose that the concealed common precursor may affect the product distribution. The initial attack of the reagent at 4a-position was previously shown.[2] Thus, the formation of the ring-opened product **(25)** showed that the most crowded internuclear 4a-position certainly reacted with V-H reagent. Furthermore, it is also strange that the benzene-part of the substrates (**5**, **6**, and **7**) seemed to be more reactive even in lower temperature than expected on usual aromatics, because usually non-activated aromatics are not so reactive[7, 8] for V-H reagents.

In the reaction of **1** with V-H reagent[2] (Scheme 1), the initially introduced 4a-substituent was finally removed by easy hydrolysis from the intermediate. Based on the concept that the reactions proceed by the same mechanism through BnTHC and the derivatives (**1**, **5**, **6**, and **7**), we propose the mechanism by which all products are produced *via* a common intermediate, using the BnTHC (1) (Scheme 7). This mechanism would solve the foregoing problems.



Scheme 7

BnTHC (**1**) initially undergoes V-H reaction at the 4a-position to give intermediate A. B, a tautomer of A, reacts with another V-H reagent at the 1-position to give intermediate C, which goes to the 1-formyl product (**2**) after hydrolysis at lower temperature, whereas goes to the aromatized compound (**3**) *via* rearrangement at a high temperature as described previously.[2] The 4a-substituent in the intermediate **C** should be removed for the formation of **2**. This means that the iminium substituent at the 4a-position is very reactive for nucleophile. On the contrary where the steric effect in the substituent (Scheme 5) and / or in reagents[3] is large as in the case of the reaction of 4,4-dimethyl-BnTHC (**7**), the reaction from B to C should be late, while intermediate A (=A') having reactive 4a-substituent, undergoes an attack of the weakly nucleophilic benzene-part of **1** to give **4** as the product and **1** as the by-product. The formation of the ring-opened product (**25**) indicates the low reactivity of the intermediate corresponding **B** going to **C** in the reaction of 4,4-dimethyl BnTHC (**7**). It cannot be denied that direct attack of the V-H reagent to the benzene-part of **1** gave **4**, in consideration of the result obtained from 1,1-dimethyl-BnTHC in Scheme 4. Or these two mechanisms may simultaneously work in the formation of the benzene-part formylated products.

ACKNOWLEDGEMENT

The authors thank the late Dr. Koreharu Ogata, Chemical Analysis Center of Chiba University, for performing X-Ray analysis of the semicarbazone of 1-benzyl-2-(4'-methyl-3'-pentenyl)indole-3-carboxaldehyde (**25**). This work was supported in part by a Grant-in-Aid for Scientific Research from the

Ministry of Education, Culture, Sports, Science and Technology of Japan.

EXPERIMENTAL

All melting points were measured on a micro melting point hot stage apparatus (Yanagimoto) and are uncorrected. IR spectra were recorded on a JASCO FT/IR-300 or on a Shimadzu IR-400 spectrometer (in Nujol, unless otherwise stated). ^{1}H-NMR spectra were measured on a Hitachi R-24B (60 MHz) unless otherwise stated, and JEOL AL 400 NMR spectrometer. Deuteriochloroform was used as the solvent with tetramethylsilane as an internal reference, unless otherwise stated. The assignments of NH signals were confirmed by disappearance of the signals after addition of deuterium oxide. MS spectra were measured on JEOL JMS-01-SG-2, JEOL JMS-D300, and JEOL JMS-DX303 spectrometers with a direct inlet system. For column chromatography, Silica gel 60 (70-230 mesh ASTM, Merck, unless otherwise stated), and for thin layer chromatography (TLC), Silica gel 60F_{254}(Merck) were used. All identifications of products were done by analysis of MS, IR spectra, and especially NMR spectra.

(9-Benzyl-1,2,3,4-tetrahydrocarbazol-1-yl)methanol (8):(9-Benzyl-1,2,3,4-tetrahydrocarbazol-1-yl)-carboxaldehyde (**2**) (5.92 g, 20.5 mmol) was stirred with $NaBH_4$ (1.51 g, 40.8 mmol) in ethanol (25 mL) at rt for 1.5 h. The reaction mixture was poured onto water (300 mL) and extracted with AcOEt. The organic layer was washed with sat. NaCl and dried over $MgSO_4$ to give colorless crystals, mp 107-110°C. *Anal*. Calcd for $C_{20}H_{21}NO$:C, 82.44;H, 7.26;N, 4.81. Found:C, 82.29;H, 7.32;N, 4.79. ^{1}H-NMR($CDCl_3$) :1.51-3.19 (7H, m, C_1, C_2, C_3, C_4-H), 3.63 (2H, d, J=6.0 Hz, -CH_2O), 5.29 (2H, s, C$\underline{H}_2$Ph), 6.67-7.81 (10 H, m, Ar-H). IR ν max(nujol) cm^{-1}:3350 (OH). MS *m/z*: 291 (M^+, 41 %), 260 (BP), 91 (73%).

(9-Benzyl-1,2,3,4-tetrahydrocarbazol-1-yl)methyl methanesulfonate (9):To a solution of (9-benzyl-1,2,3,4-tetrahydrocarbazole-1-yl)methanol (**8**) (1.17 g, 4.01 mmol) in pyridine (16 mL) was added dropwisely methanesulfonyl chloride (0.55 g, 4.82 mmol) under ice-cooling. The mixture was stirred at rt for 4.5 h, poured onto water, and extracted with benzene. The organic layer was washed with water, dried over $MgSO_4$, and evaporated to dryness. The residue (1.06 g, 72%), mp 100-103°C, was recrystallized from hexane-benzene to give colorless prisms, mp 102-104°C. *Anal*. Calcd for $C_{21}H_{23}NO_3S$:C, 68.25; H, 6.27; N, 3.79. Found: C, 68.04;H, 6.28; N, 3.74. ^{1}H-NMR($CDCl_3$) : 1.51-3.46 (7H, m, C_1, C_2, C_3, C_4-H), 2.73 (3H, s, CH_3), 4.12 (2H, d, J=7.0 Hz, -CH_2O), 5.34 (2H, s, C$\underline{H}_2$Ph), 6.76-7.62 (9H, m, Ar-H). IR ν max(nujol) cm^{-1}:1325, 1163, 934. MS *m/z*: 369 (M^+, 60%), 91 (BP).

9-Benzyl-1-methyl-1,2,3,4-tetrahydrocarbazole (5): A solution of (9-benzyl-1,2,3,4-tetrahydrocarbazol-1-yl)methyl methanesulfonate (**9**) (2.60 g, 7.05 mmol) in THF (17 mL) was added slowly to $LiAlH_4$ (0.54 g, 14.2 mmol) in a flask. The mixture was refluxed for 2 h. The reaction mixture was quenched with adding water (0.7 mL), 10%NaOH (2.6 mL), and water (3.5 mL) successively. The whole was passed through celite-column and washed thoroughly with CH_2Cl_2. The organic layer was washed with sat. NaCl and dried over $MgSO_4$. The residue (1.86 g) was column-chromatographed over silica gel using benzene-hexane (2:1) to give the target compound (**5**) as colorless product (1.77g, 91%), mp 88-95°C. Recrystallizations gave colorless prisms, mp 91-93°C. *Anal*. Calcd for $C_{20}H_{21}N$: C, 87.23;

H, 7.69; N, 5.09. Found: C, 87.41; H, 7.75; N, 5.10. ^{1}H-NMR ($CDCl_3$) δ : 1.16 (3H, d, J=7.0 Hz, -CH_3), 1.50-3.24 (7H, m, C_1, C_2, C_3, C_4-H), 5.24 (2H, s, -C$\underline{H}_2$Ph), 6.76-7.59(9H, m, Ar-H). IR ν max(nujol) cm^{-1}: no characteristic band. MS *m/z*:: 275 (M^+, 95%), 91 (BP).

9-Benzyl-1,1-dimethyl-1,2,3,4-tetrahydrocarbazole (6): A mixture of 2,2-dimethylcyclohexane [prepared from 2-methylcyclohexanone (24.77 mL)] and1-benzyl-1-phenylhydrazine hydrochloride (33.04 g, 141 mmol) in AcOH (200 mL) was refluxed for 1 h. The reaction mixture was poured onto water (300 mL), extracted with AcOEt, and the extract was washed with sat.$NaHCO_3$, and dried over $MgSO_4$. After evaporation of the solvent, the residue (41.31 g) was purified by chromatography on SiO_2 using benzene-hexane (1:10) to give colorless crystals (21.03 g, 52%). Recrystallization gave colorless plates, mp 97-98°C. *Anal*. Calcd for $C_{21}H_{23}N$: C, 87.15: H, 8.01; N, 4.84. Found: C, 87.53; H, 8.17; N, 4.73. ^{1}H-NMR(400 MHz, $CDCl_3$): 1.31 (6H, s, 2 x CH_3), 1.73-1.78 (2H, m, C_2 or C_3-H), 1.84-1.91 (2H, m, C_2 or C_3-H), 2.76 (2H, t, J=6.0 Hz, C_4-H), 5.51 (2H, s, C$\underline{H}_2$Ph), 6.92 (2H, d, J=7.0 Hz, Ar-H), 6.96-7.09 (3H, m, Ar-H), 7.16-7.27 (3H, m, Ar-H), 7.47-7.53 (1H, m, Ar-H). MS m/z: 289 (M^+), 274 (BP). IR ν max(nujol) cm^{-1}: no characteristic band.

1,2-Cyclohexadione 4,4-dimethyl-2-phenylhydrazone (14):Aniline (7.2 g, 78 mmol) was diazotized with 97% $NaNO_2$ (5.54 g, 78 mmol) in a mixture of concentrated HCl (16.74 mL, 195 mmol) and water (62 mL) under 4°C. The resulting diazonium salt solution was slowly added under 7°C to a EtOH solution of 2-hydroxymethylene-4,4-dimethylcyclohexanone[9] (11.7 g, 78 mmol) basified with 50% KOH. After stirring for 1 h under 7°C, the reaction mixture was poured into ice-water (500 mL), and the resulting precipitates (16.37 g, 91%) was collected with suction. Recrystallization from hexane gave pale yellow needles, mp 128-129°C. *Anal*. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.87; N, 12.16. Found: C, 72.51; H, 7.73; N, 11.50. IR ν max(nujol) cm^{-1}: 3220 (NH), 1660 (CO). ^{1}H-NMR ($CDCl_3$): 1.07 (6H, s, 2 x CH_3), 1.49-1.85 (2H, m, C_2-H), 2.39-2.69 (2H, m, C_1-H), 2.50 (2H, s, C_4-H), 7.20-7.51 (5H, m, Ar-H), 13.70 (1H, br s, NH). MS *m/z*: 230 (M^+, BP).

4,4-Dimethyl-1,2,3,4-tetrahydrocarbazol-1-one (15): *p*-TsOH・H_2O (16.55 g, 87 mmol) was dehydrated in Dean-Stark apparatus by refluxing in benzene (150 mL). The hydrazone (**14**) (10 g, 43.5 mmol) was added to the above solution, and the mixture was stirred at rt for 10 h. After the reaction was complete, the solvent was evaporated. The residue was dissolved in $CHCl_3$, washed with 5%$NaHCO_3$, and dried over $MgSO_4$. Evaporation of the solvent gave the residue (8.13 g), which was purified by column-chromatography over SiO_2 using benzene-AcOEt (20:1) to give red-brown crystals (9.26 g, 46%). Recrystallization from hexane gave colorless prisms, mp 153-155°C. *Anal*. Calcd for C_{14} $H_{15}NO$: C, 78.83; H, 7.03;N, 6.56. Found: C, 78.62; H, 7.14; N, 6.56. IR ν max(nujol) cm^{-1}: 3275 (NH), 1650 (CO). ^{1}H-NMR ($CDCl_3$): 1.58 (6H, s, 2 x CH_3), 1.95-2.30 (2H, m, C_3-H), 2.50-2.95 (2H, m, C_2-H), 6.90-8.01 (4H, m, Ar-H), 9.50 (1H, br s, NH). MS *m/z*: 213 (M^+), 198 (BP).

4,4-Dimethyl-1,2,3,4-tetrahydrocarbazole (16): A mixture of the ketone (**15**), KOH (1.89 g, 38 mmol), and NH_2NH_2・H_2O (1.44 g, 29 mmol) in triethylene glycol (12 mL) was heated at 200°C (bath temperature) for 4 h. After the reaction was over, water (50 mL) was added to the reaction mixture. The

mixture was extracted with ether, and the extract was dried over $MgSO_4$, and evaporated to dryness in vacuo to give the brown residue (1.44 g). The residue was purified by column-chromatography over SiO_2 using hexane:AcOEt (20:3) to give red brown crystals (1.14 g, 38 %), mp 133-135°C. Recrystallizations from AcOEt-hexane gave colorless needles, mp 138-141°C, which was used immediately for the next benzylation reaction. IR ν max(nujol) cm^{-1}: 3400 (NH). ^{1}H-NMR ($CDCl_3$): 1.42 (6H, s, 2 x CH_3), 1.61-2.10 (4H, m, C_1 and C_2-H), 2.50-2.81 (2H, m, C_3-H), 6.90-7.41 (4H, m, Ar-H), 7.65 (1H, m, NH).

9-Benzyl-4,4-dimethyl-1,2,3,4-tetrahydrocarbazole (7): A mixture of 4,4-dimethyl-1,2,3,4-tetrahydrocarbazole (**16**) (0.199 g, 1.00 mmol) and 50% NaH (0.158 g, 3.29 mmol) in anhydrous DMSO (30 mL) was stirred at rt for 1 h. To this solution was added benzyl bromide (0.237 mL, 2.0 mmol). The whole was stirred at rt for 2 h. the reaction mixture was poured onto water (100 mL) and extracted with ether. The organic solvent was washed with 5% HCl. and saturated NaCl, and dried over $MgSO_4$. Evaporation of the solvent in vacuo gave brown residue (0.451 g), which was purified with column-chromatography over SiO_2 using hexane-AcOEt (20:3) to give pale yellow-crystals (0.185 g, 63%). Recrystallization from hexane gave colorless prisms, mp 83-85°C. *Anal.* Calcd for $C_{21}H_{23}N$: C, 87.15; H, 8.01; N, 4.84. Found: C, 87.43; H, 8.12; N, 4.86. ^{1}H-NMR ($CDCl_3$): 1.48 (6H, s, 2 x CH_3), 1.68-2.15 (4H, m, C_2 and C_3-H), 2.48-2.81 (2H, m, C_1-H), 5.21 (2H, s, NCH_2Ph), 6.81-7.45 (8H, m, Ar-H), 7.55-7.90 (1H, m, C_5-H). IR ν max(nujol) cm^{-1}: no characteristic band. MS *m/z*: 289 (M^+), 274(BP).

General procedure of Vilsmeier-Haack formylation: To a solution of a 9-benzyltetrahydrocarbazole homologue (**5**, **6**, or **7**) (1 mmol) in DMF (1.95 mL) (same in a case of N-methylformanilide) was added $POCl_3$ (0.28 mL, 3 mmol) under ice-cooling. Then the reaction mixture was stirred at the desired temperature until the reaction ceased or stopped. The reaction mixture was poured onto ice-water (25 mL) and basified with K_2CO_3, and stirred for 1 h at rt. The whole was extracted with appropriate solvent (benzene or ether), and the extract was dried over $MgSO_4$, and evaporated to dryness in vacuo. The residue was chromatographed with SiO_2 with solvent (hexane, benzene, or their mixture) to give formyl products. The benzene-formylated products are described in the order of elution.

9-Benzyl-1-methyl-1,2,3,4-tetrahydrocarbazole-1-carboxaldehyde (17): Colorless oil. HRMS: Calcd for $C_{21}H_{21}NO$: 303.1624 (M^+). Found 303.1627. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.37 (3H, s, CH_3), 1.58-2.10 (4H, m, C_2 and C_3-H), 2.80-2.91 (2H, m, C_4-H), 5.19 (2H, s, $NC\underline{H}_2Ph$), 6.82 (2H, dd, J=9.0 and 2.0 Hz, Ar-H), 6.82-7.59 (9H, m, Ar-H), 9.45 (1H, s, CHO). IR ν max(nujol) cm^{-1}: 1725 (C=O). MS *m/z*: 303 (M^+, 21%), 274(BP), 91 (70%).

9-Benzyl-1-methyl-1,2,3,4-tetrahydrocarbazole-x-carboxaldehyde (18): Pale yellow oil. HRMS: Calcd for $C_{21}H_{21}NO$: 303.1624 (M^+). Found 303.1626. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.26 (3H, d, J=7.0 Hz, CH_3), 1.75-2.01 (4H, m, C_2 and C_3-H), 2.92-3.18 (3H, m, C_1 and C_4-H), 5.33-5.42 (2H, m, $C\underline{H}_2Ph$), 6.92 (2H, m, Ar-H), 7.13 (1H, t, J=8.0 Hz, C_7-H), 7.20-7.30 (3H, m, $CH_2\underline{Ph}$), 7.33 (1H, dd, J=8.0 and 2.0 Hz, C_6 or C_8-H), 7.73 (1H, dd, J=8.0 Hz and 2.0 Hz, C_6 or C_8-H), 10.60 (1H, s, -CHO). IR ν max(nujol) cm^{-1}: 1680 (C=O). MS *m/z*: 303 (M^+, 54%), 91 (BP).

9-Benzyl-1-methyl-1,2,3,4-tetrahydrocarbazole-y-carboxaldehyde (19):The compounds (**19** and **20**) were separated by liquid chromatography from their mixture and **19** was recrystallized from ether-hexane to give colorless prisms , mp 92-95°C. *Anal*. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 82.88; H, 6.99; N, 4.53. ^{1}H-NMR ($CDCl_3$): 1.21 (3H, d, J=7.0 Hz, CH_3), 1.74-2.01 (4H, m, C_2 and C_3-H), 2.64-3.03 (3H, m, C_1 and C_4-H), 5.28-5.37 (2H, m, $C\underline{H}_2Ph$), 6.93 (2H, dd, J=8.0 and 2.0 Hz, C_7-H), 7.15 (1H, d, J=8.0 Hz, C_8-H), 7.18-7.29 (3H, m, Ar-H), 7.62 (1H, dd, J=7.0 and 2.0 Hz, C_7-H), 8.05 (1H, d, J=2.0 Hz, C_6-H), 9.99 (1H, s, CHO). IR ν max(neat) cm^{-1}: 1685 (C=O). MS *m/z*: 303 (M^+, 60%), 91 (BP). HRMS: Calcd for $C_{21}H_{21}NO$:303.1624 M^+). Found: 303.1600

9-Benzyl-1-methyl-1,2,3,4-tetrahydrocarbazole-z-carboxaldehyde (20): Pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.22 (3H, d, J=7.0 Hz, CH_3), 1.74-2.00 (4H, m, C_2 and C_3-H), 2.63-3.06 (3H, m, C_1 and C_4-H), 5.33-5.43 (2H, m, $C\underline{H}_2Ph$), 6.92 (2H, dd, J=8.0 and 2.0 Hz, Ar-H), 7.18-7.29 (3H, m, Ar-H), 7.57 (1H, d, J=8.0 Hz, C_5-H), 7.60 (1H, dd, J=8.0 and 2.0 H, C_6-H), 7.65 (1H, d, J=2.0 Hz, C_8-H), 9.92 (1H, s, -CHO). IR ν max(neat) cm^{-1}: 1680 (C=O). MS *m/z*: 303 (M^+, 52%), 91 (BP). HRMS: Calcd for $C_{21}H_{21}$ NO: 303.1624 (M^+). Found: 303.1617.

9-Benzyl-1,1-dimethyl-1,2,3,4-tetrahydrocarbazole-x-carboxaldehyde (21):Pale yellow prisms, mp 87-92°C (Et_2O-hexane). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.37 (6H, s, 2 x CH_3), 1.76-1.95 (4H, m, C_2 and C_3-H), 3.06 (2H, m, C_4-H), 5.59 (2H, s, $C\underline{H}_2Ph$), 6.89 (2H, m, Ar-H), 7.11 (1H, t, J=8.0 Hz, C_7-H), 7.19-7.31 (4H, m, Ar-H), 7.73 (1H, m, C_6-H), 10.60 (1H, s, -CHO). IR ν max(nujol) cm^{-1}: 1690 (C=O). MS *m/z*: 317 (M^+,), 91 (BP). HRMS: Calcd for $C_{22}H_{23}NO$: 317.1780. Found: 317.1746.

A mixture of **9-benzyl-1,1-dimethyl-1,2,3,4-tetrahydrocarbazole-y and -z-carboxaldehyde (22 and 23)** :Pale yellow oil. IR ν max(nujol) cm^{-1}: 1690 (C=O). ^{1}H-NMR (400 MHz, $CDCl_3$) (estimated the larger $C\underline{H}O$ as 1H): 1.33(6H, s, 2 x CH_3), 1.76-2.82 (7.5H, m, C_2, C_3, and C_4-H), 5.55 (0.5H, s, $C\underline{H}_2Ph$), 5.60 (2H, s, $C\underline{H}_2Ph$), 6.88-8.05 (10.1H, m, arom H), 9.90 (1H, s, CHO), 10.00 (0.26H, s, CHO). MS *m/z*: 317 (M^+,), 91 (BP). HRMS: Calcd for $C_{22}H_{23}$ NO: 317.1780. Found: 317.1778.

9-Benzyl-4,4-dimethyl-1,2,3,4-tetrahydrocarbazole-1-carboxaldehyde (24): Colorless oil. *Anal*. Calcd for $C_{22}H_{23}NO$: C, 83.33; H, 7.31; N, 4.42. Found: C, 83.22; H, 7.38; N, 4.21. IR ν max(nujol) cm^{-1}: 1708 (C=O). ^{1}H-NMR ($CDCl_3$): 1.42 (3H, s, CH_3), 1.53 (3H, s, CH_3), 1.54-2.37 (4H, m, C_2 and C_3-H), 3.49 (1H, br s, C_1-H), 5.23 (2H, s, -$C\underline{H}_2Ph$), 6.70-7.38 (8H, m, Ar-H), 7.75 (1H, m, C_5-H), 9.55 (1H, d, J=3.0 Hz, -CHO). MS *m/z*: 317 (M^+), 91 (BP).

1-Benzyl-2-(4'-methyl-3'-pentenyl)indole-3-carboxaldehyde (25): Colorless oil. IR ν max(nujol) cm^{-1}: 1650 (C=O). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.43 (3H, s, CH_3), 1.66 (3H, s, CH_3), 2.56 (2H, m, $C_{2'}$-H), 3.07 (2H, m, $C_{1'}$-H), 5.15 (1H, m, $C_{3'}$-H), 5.39 (2H, s, -$C\underline{H}_2Ph$), 7.00 (2H, m, Ar-H), 7.19-7.32 (6H, m, Ar-H), 8.20-8.40 (1H, m, Ar-H), 10.20 (1H, s, -CHO). MS *m/z*: 317 (M^+), 91 (BP).

Semicarbazone of 25: To a solution of **25** (92 mg, 0.29 mmol) in EtOH (1 mL) was added a mixture of semicarbazide hydrochloride (37 mg, 0.32 mmol) and AcONa・$3H_2O$ (44 mg, 0.32 mmol) in 50% EtOH (1 mL). The mixture was allowed to stand at rt for 2 days. After the reaction was over, the precipitates

(89 mg) were collected with suction, and recrystallized from hexane-AcOEt to give colorless needles (77 mg, 71%), mp 159.5-163°C. *Anal*. Calcd for $C_{25}H_{32}N_4O_2 \cdot C_2H_5OH$: C, 71.40; H, 7.67; N, 13.32. Found: C, 71.39; H, 7.67; N, 13.32. IR ν max(nujol) cm^{-1}: 3459 (NH), 1682 (C=O). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.38 (3H, m, CH_3), 1.62 (3H, m, CH_3), 1.82-2.38 (2H, m, $C_{2'}$-H), 2.55-3.05 (2H, m, $C_{1'}$-H), 5.00 (1H, br s, $C_{3'}$-H), 5.10 (2H, s, -C<u>H</u>$_2$Ph), 5.92 (2H, s, NH_2), 6.60-7.40 (8H, m, Ar-H and <u>H</u>C=N-), 8.06 (2H, m, Ar-H), 10.01 (1H, s, NH). The signals due to C_2H_5OH were excluded.

A part of the mixture of 9-benzyl-4,4-dimethyl-1,2,3,4-tetrahydrocarbazole-x-carboxaldehyde (**26**) and 9-benzyl-4,4-dimethyl-1,2,3,4-tetrahydrocarbazole-y-carboxaldehyde **(27**) was separated into each components by repeated column-chromatography [SiO_2, hexane-AcOEt (10:1)].

9-Benzyl-4,4-dimethyl-1,2,3,4-tetrahydrocarbazole-x-carboxaldehyde (26): Colorless prisms, mp 126-129°C from hexane-AcOEt. *Anal*. Calcd for $C_{22}H_{23}NO$: C, 83.33; H, 7.31; N, 4.42. Found: C, 82.95; H, 7.35; N, 4.28. IR ν max(nujol) cm^{-1}:1679 (C=O). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.44 (6H, s, 2 x CH_3), 1.63-1.68 (2H, m, C_3-H), 1.81-1.89 (2H, m, C_2-H), 2.54 (2H, m, C_1-H), 5.22 (2H, s, -C<u>H</u>$_2$Ph), 6.89-6.94 (2H, m, Ar-H), 7.17-7.27 (4H, m, Ar-H), 7.60 (1H, dd, J=8.0 and 2.0 Hz, C_7-H), 8.19 (1H, d, J=2.0 Hz, C_5-H), 9.97 (1H, s, -CHO). MS *m/z*: 317 (M^+), 91 (BP).

9-Benzyl-4,4-dimethyl-1,2,3,4-tetrahydrocarbazole-y-carboxaldehyde (27): Colorless prisms from hexane-AcOEt, mp 129-132°C. Anal. Calcd for $C_{22}H_{23}NO$: C, 83.33; H, 7.31; N, 4.42. Found: C, 83.03; H, 7.31; N, 4.35. IR ν max(nujol) cm^{-1}:1671 (C=O). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.46 (6H, s, 2 x CH_3), 1.67-1.72 (2H, m, C_3-H), 1.86-1.93 (2H, m, C_2-H), 2.62 (2H, t, C_1-H), 5.31 (2H, s, -C<u>H</u>$_2$Ph), 6.96 (2H, m, arom H), 7.21-7.31 (3H, m, arom H), 7.69 (1H, dd, J=8.0 and 2.0 Hz, C_6-H), 7.77 (1H, d, J=2.0 Hz, C_8-H), 7.80 (1H, d, J=8.0 Hz, C_5-H), 9.96 (1H, s, -CHO). MS *m/z*: 317 (M^+), 91 (BP).

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