EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201800187

Link to VoR: http://dx.doi.org/10.1002/ejoc.201800187

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10.1002/ejoc.201800187

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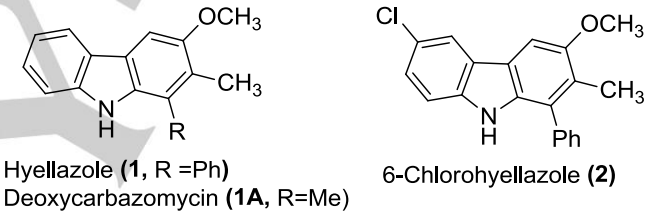
Total Synthesis of Marine Alkaloid Hyellazole and Its Derivatives

Suchandra Chakraborty*[a] and Chandan Saha[b]

Abstract: Total syntheses of naturally occurring marine alkaloids Hyellazole and chlorohyellazole is attempted from easily accessible corresponding 2-methyl-1-ketotetrahydrocarbazoles incurred through Japp-Klingeman reaction followed by Fischer indole cyclization and then Grignard reaction using phenyl magnesium bromide in sequence. Although Grignard reaction on 2-methyl-1-ketotetrahydrocarbazole leads directly to furnish 1-phenyl-2-methylcarbazole through dehydration followed by aromatization through aerial oxidation, the same reaction on 6-chloro-2-methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one through careful treatment leads to the isolation of 6-chloro-2-methyl-1-phenyl-4,9-dihydro-3*H*-carbazole. However selenium dioxide oxidation of this dihydrochloroderivative leads to the formation of 6-chloro-2-methyl-1-phenyl-9*H*-carbazole. A different route is then adopted using suitably substituted aromatic amine to arrive at the substitution pattern of required carbazole derivative with a bromo group at C-1 and the required phenyl group at 1-postion is then fabricated through Suzuki-Miyaura cross-coupling to furnish Hyellazole.

Introduction

Over past 40 years[1-6] a vast number of carbazole alkaloids have mostly been isolated from terrestrial plants. Other than this, a large number of carbazole alkaloids have been encountered in different algae and streptomycillin species.[2] In 1979 Hyellazole and 6-chlorohyellazole (Figure 1) were the first carbazole alkaloids isolated from the blue-green alga *Hyella caespitosa,* a marine sources by Moore.[7] Although these two alkaloids have different in origin, yet these are structurally unique having a methoxy group at 3-position like some other carbazole alkaloids along with a phenyl group at 1-position. Interesting structural features of these alkaloids allured several research groups to spring up different route for their total synthesis. Since the isolation of these alkaloids more than fifteen different methods of total syntheses[8-18] were originated for them till date. Kano et al. in 1981 have synthesized[8] both hyellazole and 6-chlorohyellazole from the correspondding 2,3-divinylindoles through thermal electrocylic ring closure followed dehydrogenation with palladised charcoal *in situ*. Later on in 1989 Kawasaki et al.[10] have utilized unique electrocylic ring closure procedure on properly substituted 3-butadienylindoles to obtain carbazole moiety which on subsequent desilylation yielded hyellazole. Moddy et al.[11] have subsequently published a versatile route to polysubstituted carbazoles based on Diels-Alder reaction on pyrano[3,4-*b*]indol-3-ones with alkynes and this concept was utilized to obtain hyellazole in a short route. Knoelkar et al. developed a highly convergent scheme to 3-oxygenated carbazole alkaloids, in which heterocyclic framework was constructed by a successive iron-mediated C—C and C—N bonds formation and this method was established to be useful for the synthesis of hyellazole[14] and 6-chlorohyellazole.[18] In 1996 Hibino et al.[15] have synthesized hyellazole by a new type allene mediated electrocyclic ring closure with the participation of indole 2,3-double bond. Here we have developed a very simple strategy to synthesis the marine alkaloid, hyellazole in which heterocyclic framework is constructed via consecutive Fischer indole cyclization and aromatization and required phenyl group is fabricated at the 1-position through Suzuki-Miyaura cross-coupling.[19]



Hyellazole **(1,** R =Ph**)**
Deoxycarbazomycin **(1A,** R=Me**)**

6-Chlorohyellazole **(2)**

Figure 1. Naturally occurring marine alkaloids.

As an extension of this Suzuki-Miyaura cross-coupling reaction is utilized to afford 4-deoxycarbazomycin B (**1A**).[20a]

Results and Discussion

Initial Synthetic Plan for Hyellazole and 6-Chlorohyellazole

Our laboratory is well conversant about the chemistry of 1-ketotetrahydrocarbazole derivatives which are easily procurable through Japp-Klingeman reaction between diazonium chloride and 2-formylcyclohexanone derivatives followed by Fischer indole cyclization.[20] As a result we are interested to synthesize hyellazole (**1**) and 6-chlorohyellazole (**2**) through the treatment of phenyl magnesium bromide on 2-methyl-1-ketotetrahydrocarbazoles (**3a** and **3b**) followed by dehydration to yield 2-methyl-1-phenyl-3,4-dihydrocarbazoles (**4a** and **4b**) which on allylic oxidation and functional group interconversion may lead to the target molecules (Scheme 1).

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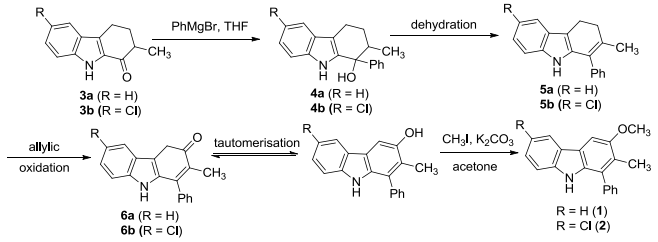
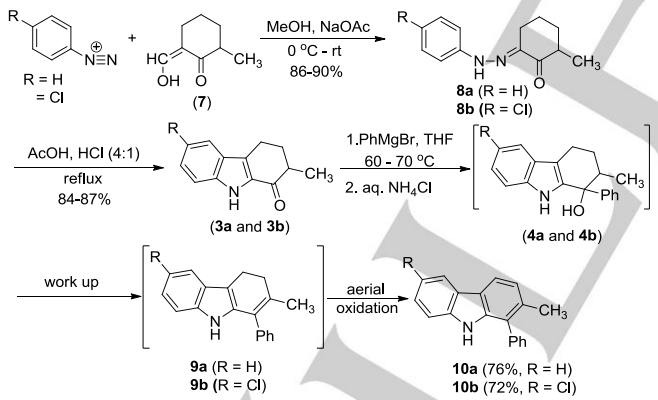
Supporting information for this article is available.



Scheme 1. Proposed plan to synthesize Hyellazole (1) and 6-Chlorohyellazole (**2**).

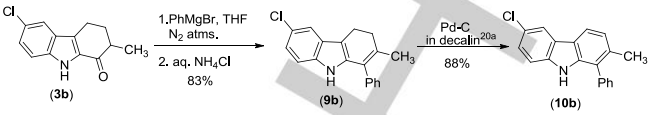
Actual Observation

To accomplish our target 2-methyl-1-ketotetrathydrocarbazole (**3a**) and 6-chloro-2-methyl-1-ketotetrathydrocarbazole (**3b**) were synthesized from aniline and *p*-chloroaniline respectively through diazotization followed by Japp-Klingeman coupling with 2-formyl-6-methylcyclohexanone (**7**) followed by Fischer indole cyclization[20] on the corresponding 2-methyl-(6-phenylhydrazono)cyclohexanaones (**8a** and **8b**) respectively. Now these substituted 2-methyl-1-ketotetrahydrocarbazoles (**3a** and **3b**) on treatment with phenyl magnesium bromide yielded directly 2-methyl-1-phenyl-carbazoles (**10a** and **10b**) wherein it may be speculated that during work up with aqueous ammonium chloride the possible intermediates **4a** and **4b**, the benzyl alcohols experience dehydration to **9a** and **9b** respectively which undergoes aerial oxidation directly to furnish **10a** and **10b** (Scheme 2) respectively.



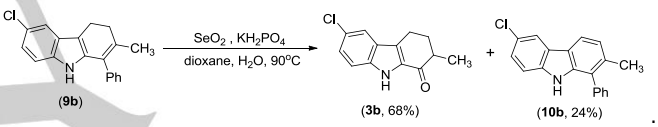
Scheme 2. Grignard Reaction on 2-methyl-1-ketotetrahydrocarbazole derivatives (**3a**) and (**3b**)

However, yet cautious handling of phenyl magnesium bromide reaction on **3a** under inert atmosphere, it was unsuccessful to isolate highly unstable dehydrated product **9a** which is extremely susceptible to aerial oxidation. On the contrary, Grignard reaction in inert atmosphere on **3b** it was possible to isolate stable dehydrated product **9b** whose structure was confirmed through ^{1}H and ^{13}C-NMR spectra. In addition, **9b** on treatment with Pd-C aromatized[20a] the ring to the corresponding chlorohyellazole derivative **10b** (Scheme 3).



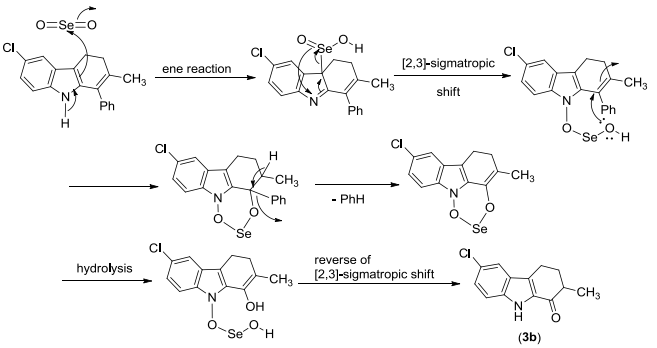
Scheme 3. Grignard Reaction on 2-methyl-6-choloro-1-ketotetrahydrocarbazoles (**3b**) under inert atmosphere

Now according the proposed Scheme 1, as it was possible to synthesis **9b**, it is then allowed to meet with selenium dioxide to execute the allylic oxidation[21] followed by *O*-methylation to furnish 6-chlorohyellazole. However, selenium dioxide oxidation of **9b** surprisingly turned back to the starting material 2-methyl-6-choloro-1-ketotetrahydrocarbazoles (**3b**) with the expulsion of phenyl motif as a major product along with minor amount of aromatized demethoxychlorohyellazole **10b** (Scheme 4)



Scheme 4. Attempted selenium dioxide oxidation of 6-chloro-2-methyl-1-phenyl-4,9-dihydro-3*H*-carbazole (**9b**)

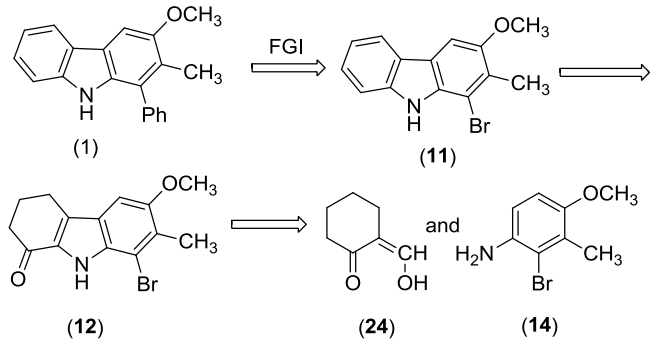
The plausible steps for the selenium (IV) oxide mediated reaction might be taken place through an ene reaction followed by sigatropic [2,3]-rearrangement of intermediate selenium (IV) acid to yield selenium (II) acid.[22] This selenium (II) acid then undergoes electrophilic addition at the carbon-carbon double bond to yield an intramolecular ester from which benzene is eliminated to restore the double bond at its initial location. The intermediate then hydrolyzed and a reverse of sigatropic [2,3]-rearrangement proceeds to furnish **3b** (Scheme 5).



Scheme 5. Plausible mechanism of the selenium dioxide oxidation to furnish **3b**

Modified Retrosynthetic Analysis

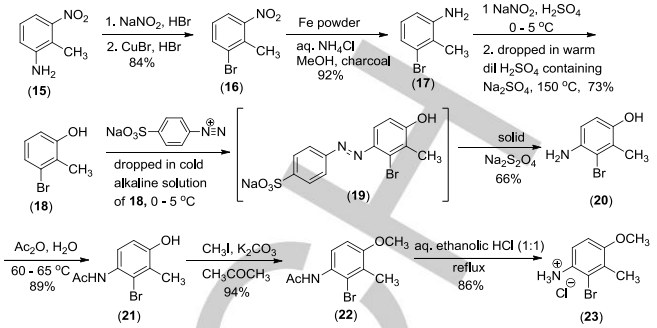
This disappointment motivated us to synthesize Hyellazole through a different route where it is thought that suitably substituted aromatic amine may be employed to acquire the precise substitution pattern of Hyellazole and the necessitated phenyl group at 1-postion will be incorporated through Suzuki cross-coupling on the corresponding 1-boromocarbazole (**11**). Required 1-bromocarbazole (**11**) may be synthesized through the Japp-Klingeman reaction directly from the corresponding amine (**14**) and 2-formylcyclohexanone (**24**) followed by Fischer indole cyclization and aromatization (Scheme 6).



Scheme 6. Retrosynthetic analysis for the synthesis of Hyellazole

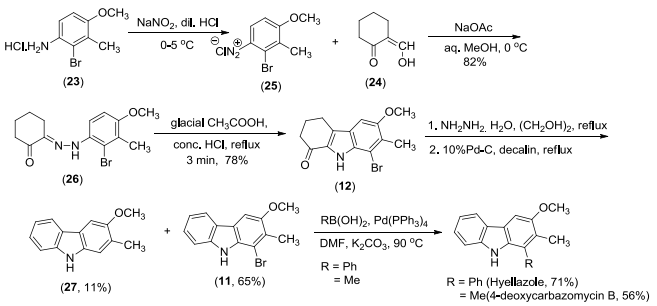
Total Synthesis of Hyellazole

On the basis of the above retrosynthetic analysis a convergent synthesis of the target molecule (**1**) was initiated from the commercially accessible 2-methyl-3-nitroaniline (**15**), which on Sandmeyer reaction[23] led to the formation of 2-methyl-3-nitrobromobenzene (**16**). This bromo compound (**16**) was on simple reduction with iron powder in aqueous methanolic ammonium chloride provided 3-bromo-2-methylaniline (**17**). The amino group of **17** was then altered[24] to phenolic hydroxyl group through diazotization to incur 3-bromo-2-methylphenol (**18**). The essential amino group at the *para*-position with respect to phenolic hydroxyl group of **18** was incorporated through[25] the classical diazo-coupling with diazotized 4-aminobenzenesulfonic acid and then subsequent reduction of **19** by means of commercially cheap sodium dithionate to furnish 4-amino-3-bromo-2-methylphenol (**20**). Required amine hydrochloride (**23**) was then synthesized from **20** on protecting the amino group via acetylation, *O*-methylation followed by hydrolysis of acetamide derivative (**22**) with aqueous ethanolic hydrochloric acid (Scheme 7).



Scheme 7. Synthesis of 2-bromo-4-methoxy-3-methylaniline hydrochloride (**23**)

Afterwards the convergent synthesis of **12** was initiated by means of Claisen condensation[26] of cyclohexanone with ethyl formate utilizing metallic sodium in dry ether in presence of one drop of ethanol to afford 2-formylcyclohexanone (**24**) which was then undergo Japp-Klingemann coupling with 2-bromo-4-methoxy-3-methylbenzene diazonium chloride (**25**) to furnish substituted phenylhydrazonocyclohexanone (**26**). Fischer indole cyclization[26] of **26** in glacial acetic acid and conc. hydrochloric acid mixture yielded 1-ketotetrahydrocarbazole (**12**). Then the Wolff-Kishner reduction of this 1-ketotetrahydrocarbazole derivative (**12**) followed by aromatization[27] without isolating the intermediate tetrahydrocarbazole derivative using 10% palladized charcoal afforded the mixture of 3-methoxy-2-methyl-9*H*-carbazole (**27**) with 11% yield and 1-bromo-3-methoxy-2-methyl-9*H*-carbazole (**11**) as 65% yield. At the final stage 1-bromo-3-methoxy-2-methyl-9*H*-carbazole (**11)** was subjected to Suzuki cross-coupling[28] with phenylboronic acid and methylboronic acid respectively in presence of palladium catalyst to afford hyellazole (**1,** 71% yield) and 4-deoxycarbazomycin B (**1A,** 56% yield) (Scheme 8).



Scheme 8. Synthesis of Hyellazole and 4-deoxycarbazomycin B

Conclusions

We have achieved the total synthesis of hyellazole as well as 4-deoxycarbazomycin B from an easily available starting material, 2-methyl-3-nitroaniline. Required amine hydrochloride was synthesized from 2-methyl-3-nitroaniline utilizing common

classical reactions through eight possible steps. Subsequent Japp-Klingemann coupling of 2-formylcyclohexanone with 2-bromo-4-methoxy-3-methylbenzene diazonium chloride followed by Fischer indole cyclization and aromatization afforded 1-bromo-3-methoxy-2-methyl-9*H*-carbazole. Finally Suzuki-Miyaura cross-coupling of 1-bromo-3-methoxy-2-methyl-9*H*-carbazole with phenylboronic acid and methylboronic acid respectively in presence of palladium catalyst afforded hyellazole and 4-deoxycarbazomycin B.

Experimental Section

General Methods: All reactions were carried out using anhydrous solvents. Melting points were determined in open capillaries in melting point instrument and are uncorrected. Reagent grade chemicals were purchased from commercial sources and used without further purification. Column chromatography was performed to obtain pure compounds using silica gel (60 - 120 mesh). All reaction mixtures and column eluents were monitored by TLC using commercial aluminium TLC plates (Merck Kieselgel 60 F254). The plates were observed under UV light at 254 and 365 nm. The structure of known compounds was further corroborated by comparing their ^{1}H NMR, ^{13}C NMR data and MS data with those in literature. IR spectra were recorded in KBr discs with a Shimadzu FTIR-8300 spectrophotometer, and ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AV 300 MHz and 400 MHz instrument. High-resolution mass spectra (HRMS) were performed with a QTOF Micro YA263 instrument.

3-Methyl-2-oxocyclohexanecarbaldehyde (7)[26]: A solution of 2-methylcyclohexanone (11.2 g, 0.1 mol) and ethyl formate (18.0 mL, 0.15 mol) in sodium dried diethyl ether (200 mL) was taken in a conical flask (500 mL) with a magnetic stirrer and $CaCl_2$ guard tube and placed it in a cold water bath. To start Claisen condensation, metallic sodium (2.3 g, 0.1 mol) and five drops of ethanol were added to the stirred mixture and stirring was continued for 4 hr, whereupon the sodium salt of 3-methyl-2-oxocyclohexanecarbaldehyde was separated as a cake-like mass. To remove some unused metallic sodium ethanol (5 mL) was added, and the mixture was stirred for an additional 30 min. Sodium salt of 3-methyl-2-oxocyclohexanecarbaldehyde was then dissolved in water (150 mL) and the aqueous layer was collected. The organic layer was further extracted with water (50 mL) and the combined aqueous extract was washed with diethyl ether (50 mL). The aqueous layer was then acidified with 6(N) hydrochloric acid (8.0 mL) and oily organic part was extracted with diethyl ether (2×80 mL). The organic layer was then washed with brine and dried over anhydrous sodium sulfate. The organic layer, on evaporation followed by vacuum distillation (70 °C, 0.5 Torr), gave product **7** (10 g, 70% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (d, J = 7.0 Hz, 3H, CH_3), 1.37–1.42 (m, 1H), 1.57–1.60 (m, 1H), 1.76–1.80 (m, 1H), 1.85–1.89 (m, 1H), 2.32–2.35 (m, 2H), 2.45–2.49 (m, 1H), 8.60 (s, 1H, CHO), 14.55 (br. s, 1H, enol-OH) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 17.4 (CH_3), 20.9 (CH_2), 23.7 (CH_2), 30.0 (CH_2), 35.8 (CH), 108.3 (CH), 187.0 (C), 188.6 (C) ppm. HRMS (QTOF): calcd. for $C_8H_{13}O_2$ $[M + H]^+$ 141.0912; found 141.0917.

2-Methyl-6-(2-phenylhydrazono)cyclohexanone (8a)[26] and 2-Methyl-6-[2-(4-chlorophenyl)hydrazono]cyclohexanone (8b): To a solution of **7** (14 g, 0.1 mol) in methanol (160 mL), aqueous solution (80 mL) of sodium acetate trihydrate (20 g) was added and it was cooled to 0 °C. Then a solution of phenyldiazonium chloride (prepared from 0.1 mol aniline) was allowed to add in drop-wise manner with stirring. The yellow solid **8a**, thus formed, was collected by filtration and washed with water. This on crystallization from aqueous methanol **8a** (18.5 g, yield 86%) was obtained as yellow crystals; m.p. 98 °C (ref.[26] 97 °C); R_f = 0.8 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (d, J = 7.0 Hz, 3H, CH_3), 1.51–2.78 (m, 7H, 2 × 3-H, 2 × 4-H, 2 × 5-H, 2-H), 6.98 (d, J =7.5 Hz, 2H, Ar-H), 7.21–7.30 (m, 3H, Ar-H), 13.71 (s, 1H, NH; exch.) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 14.8 (CH_3), 16.3 (CH_2), 22.0 (CH_2), 31.6 (CH_2), 43.7 (CH), 114.3 (CH), 122.8 (CH), 125.9 (CH), 128.9 (CH), 129.4 (CH), 132.2 (C), 143.3 (C), 200.1 (C=O) ppm. IR spectrum (KBr): v = 3495 (br), 3292, 2965, 1678, 1620, 1536, 1498, 1442 cm^{-1}. UV/Vis (MeOH): λ^{max} = 236, 300, 358 nm. HRMS (Q-TOF): calcd. for $C_{13}H_{16}N_2ONa$ $[M + Na]^+$ 239.1154; found 239.1156.

Similarly **8b** was prepared in analogous way utilizing 4-chlorophenyl diazonium chloride (prepared from 0.1 mol, 12.75 g *p*-chloroaniline) in place of phenyldiazonium chloride. The crude product on crystallization from aqueous methanol afforded **8b** (22.5 g, yield 90%) as yellow solid; m.p. 91 °C R_f = 0.8 (benzene/chloroform/diethylamine,14:5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23 (d, J = 3.0 Hz, 3H, CH_3), 1.52–2.76 (m, 7H, 2 × 3-H, 2 × 4-H, 2 × 5-H, 2-H), 6.97 (d, J =8.0 Hz, 2H, Ar-H), 7.22 (d, J =8.0 Hz, 2H, Ar-H), 13.70 (s, 1H, NH; exch.) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 14.6 (CH_3), 16.3 (CH_2), 22.0 (CH_2), 30.5 (CH_2), 43.4 (CH), 114.2 (CH), 122.6 (CH), 125.8 (CH), 128.8 (CH), 129.4 (C), 132.2 (C), 142.3 (C), 198.1 (C=O) ppm. IR spectrum (KBr): v = 3493 (br), 3295, 2897, 1682, 1618, 1545, 1445 cm^{-1}. UV/Vis (MeOH): λ^{max} = 242, 310, 362 nm. HRMS (Q-TOF): calcd. for $C_{13}H_{15}N_2OClNa$ $[M + Na]^+$ 273.0764; found 273.0768.

2-Methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one (3a)[26] and 6-Chloro-2-methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one (3b): A solution of **8a** (10.8 g, 0.05 mol) in glacial acetic acid (80 mL) containing conc. hydrochloric acid (20 mL) was heated to reflux for 4 min. The reaction mixture was poured into ice-water (300 mL) and the solid thus obtained was collected by filtration, washed with water, and dried. The residue was subjected to flash chromatography (hexane/CH_2Cl_2, 7:3) on silica gel to give a white solid. Recrystallization of the solid from dichloromethane/hexane provided **3a** (8.4 g, yield 84%) as white crystals; m.p. 172–173 °C (ref.[26] 173 °C); R_f = 0.7 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (d, J = 8.0 Hz, 3H, CH_3), 2.02 (m, 1H, C3-H), 2.32 (m, 1H, C3-H), 2.72 (m, 1H, C2-H), 2.97 (m, 1H, C4-H), 3.09 (m, 1H, C4-H), 7.13 (t, 1H, Ar-H), 7.35 (t, 1H, Ar-H), 7.46 (d, J = 8.5 Hz, 1H, Ar-H), 7.64 (d, J = 8.5 Hz, 1H, Ar-H), 9.68 (s, 1H, NH; exch) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2 (CH_3), 20.6 (CH_2), 33.2 (CH_2), 41.9 (CH), 112.7 (CH), 120.2 (CH), 121.2 (CH), 125.8 (CH), 126.8 (C), 129.0 (C), 130.9 (C), 138.3 (C), 194.5 (C=O) ppm. IR spectrum (KBr): v = 3284, 2932, 1688, 1516, 1492 cm^{-1}. UV/Vis (MeOH): λ^{max} = 238, 312 nm. HRMS (Q-TOF): calcd. for $C_{13}H_{13}NONa$ $[M + Na]^+$ 222.0890; found 222.0892.

Similar Fischer Indole Cyclization of **8b** (12.5 g, 0.05 mol) in glacial acetic acid (100 mL) containing conc. hydrochloric acid (25 mL) led to the formation of 6-chloro-2-methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one (**3b**) which on flash chromatography (hexane/CH_2Cl_2, 7:3) on silica gel provided **3b** (10.1 g, yield 87%) as white crystals; m.p. 198 °C. R_f = 0.6 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (d, J = 6.9 Hz, 3H, CH_3), 1.98-2.08 (m, 1H, C3-H), 2.30-2.36 (m, 1H, C3-H), 2.70-2.75 (m, 1H, C2-H), 2.93-3.06 (m, 2H, C4-H), 7.30 (d, J = 8.5 Hz, 1H, Ar-H), 7.41 (d, J = 8.7 Hz, 1H, Ar-H), 7.6 (s, 1H, Ar-H), 10.06 (s, 1H, NH; exch) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.3 (CH_3), 20.6 (CH_2), 33.2 (CH_2), 42.1 (CH), 114.0 (CH), 120.5 (CH), 126.0 (CH), 126.7 (C), 127.3 (C), 128.4 (C), 132.0 (C), 136.7 (C), 194.9 (C=O) ppm. IR spectrum (KBr): v = 3286, 2930, 1685, 1518, 1490 cm^{-1}. UV/Vis (MeOH): λ^{max} = 236, 315 nm. HRMS (Q-TOF): calcd. for $C_{13}H_{12}NOClNa$ $[M + Na]^+$ 256.0500; found 256.0503.

2-Methyl-1-phenyl-9*H*-carbazole (10a) and 6-Chloro-2-methyl-1-phenyl-9*H*-carbazole (10b): Magnesium turnings (270.0 mg, 10.0 mmol) and a few crystals (2-3) of iodine were taken in a round bottom flask and warmed to activate the Mg. To it 5.0 mL. dry tetrahydrofuran (THF), 1,2-dibromoethane (5 drops) were placed and stirred at room temperature. Bromobenzene (1.05 mL., 10 mmol) was taken in 10.0 mL dry THF. Initially 3.0 mL solution of boromobenzene was added to the reaction mixture and warmed at 60-70 °C. When the reaction mixture started to boil remaining solution of bromobenzene was added to it and the reaction mixture was allowed to boil for about 30 min. Afterwards the solution of 2-methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one **(3a,** 995.0 mg, 5.0 mmol) in dry THF (15 mL) was added in drop-wise manner to the hot solution of Grignard reagent with stirring only and then allowed to come at room temperature within 1 hr. Saturated aqueous solution of NH_4Cl (45 mL) was added to the reaction mixture with stirring for about 1 hr. The reaction mixture was then extracted with ether (5 × 40 mL) and then the ether layer was washed with brine solution (2 × 20 mL) followed by water (1 × 30mL). Ether solution was then dried over anhydrous Na_2SO_4. After evaporation of ether, the product was flash chromatographed over silica gel and eluted with hexane:dicholromethane (50:1) to obtain 2-methyl-1-phenyl-9*H*-carbazole (**10a**, 976.6 mg, yield 76%) as white crystals.

2-Methyl-1-phenyl-9*H*-carbazole (10a): m.p. 102 °C; R_f = 0.9 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.37 (s, 3H, CH_3), 7.19 – 7.26 (m, 2H, Ar-H), 7.31 (d, J = 7.5 Hz, 1H, Ar-H), 7.36 (t, 1H, Ar-H), 7.47 (t, 3H, Ar-H), 7.56 (t, 2H, Ar-H), 7.97 (d, J = 8.0 Hz, 1H, Ar-H), 8.07 (d, J = 7.5 Hz, 1H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.2 (CH_3), 110.6 (CH), 118.8 (C), 119.2 (CH), 119.4 (CH), 120.2 (CH), 121.2 (C), 122.1 (CH), 123.8 (C), 125.4 (CH), 127.7 (CH), 129.2 (2×CH), 129.9 (2×CH), 133.2 (C), 137.7 (C), 138.9 (C), 139.5 (C) ppm. IR spectrum (KBr): v = 3396, 3055, 3026, 2918, 1604 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{19}H_{15}NNa$ $[M + Na]^+$ 280.1097; found 280.1099.

Similar Grignard reaction on 6-chloro-2-methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one (**3b**, 1.16 g, 5 mmol) with phenylmagnesium bromide afforded 6-Chloro-2-methyl-1-phenyl-9*H*-carbazole (**10b**, 1.04 g, yield 72%) as white crystals.

6-Chloro-2-methyl-1-phenyl-9*H*-carbazole (10b): m.p. 99 °C; R_f = 0.8 (benzene/chloroform/diethylamine, 14:5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.33 (s, 3H, CH_3), 7.15 – 7.21 (m, 2H, Ar-H), 7.26 (d, J = 8.5 Hz, 1H, Ar-H), 7.32 (t, 1H, Ar-H), 7.40 – 7.45 (m, 2H, Ar-H), 7.53 (t, 2H, Ar-H), 7.92 (d, J = 8.0 Hz, 1H, Ar-H), 8.02 (d, J = 7.5 Hz, 1H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2 (CH_3), 111.6 (CH), 117.5 (CH), 119.3 (CH), 120.4 (CH), 121.0 (C), 122.5 (CH), 124.9 (C), 125.5 (CH), 127.3 (C), 127.7 (CH), 128.8 (CH), 129.6 (CH), 129.7 (CH), 129.9 (C), 134.0 (C), 134.2 (C), 136.9 (C), 137.4 (C) ppm. IR spectrum (KBr): v = 3400, 3026, 2916, 2858, 1604 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{19}H_{14}NClNa$ $[M + Na]^+$ 314.0707; found 314.0706.

6-chloro-2-methyl-1-phenyl-4,9-dihydro-3*H*-carbazole (9b): Magnesium turnings (540.0 mg, 20.0 mmol) and a few crystals (2-3) of iodine were taken in a two necked round bottom flask and warmed to activate the Mg. To it 6.0 mL. dry THF, 1,2-dibromoethane (6-8 drops) were placed and the flask was flashed with nitrogen gas followed by stirred at room temperature in N_2-atmosphere. Then in an another flask bromobenzene (2.1 mL., 20 mmol) was taken in 15.0 mL dry THF. Initially 5.0 mL solution of boromobenzene was injected to the reaction mixture through stoppered inlet of the flask and warmed at 70-80 °C under inert condition. When the reaction mixture started to boil remaining solution of bromobenzene was injected to it and the reaction mixture was allowed to boil for about 30 min. Afterwards the solution of 2-methyl-2,3,4,9-tetrahydro-*1H*-carbazol-1-one **(3a,** 2.3 g, 10.0 mmol) in dry THF (20.0 mL) was added in drop-wise manner to the hot solution of Grignard reagent with stirring only and then allowed to come at room temperature within 1 hr. maintaining the inert atmosphere throughout. Then with the cautious handling saturated aqueous solution of NH_4Cl (45 mL) was added to the reaction mixture and stirred for about 1 hr under N_2-atmosphere. The reaction mixture was then extracted with ether (5 × 40 mL) and then the ether layer was washed with brine solution (2 × 20 mL) followed by water (1 × 30mL). Ether solution was then dried over anhydrous Na_2SO_4. After evaporation of ether, the product, 6-chloro-2-methyl-1-phenyl-4,9-dihydro-3*H*-carbazole (**9b**, 2.4 g, yield 83%) was obtained. It was recrystallized from hexane-dichloromethane mixture to furnish white crystals; m.p. 98 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85 (s, 3H, CH_3), 2.63 (t, 2H, C3-CH_2), 2.94 (t, 2H, C4-CH_2), 6.99 (dd, J = 1.8 Hz, J = 2.1 Hz, 2H, Ar-H), 7.26 – 7.31 (m, 3H, Ar-H), 7.39 – 7.49 (m, 3H, Ar-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 (CH_3), 20.6 (CH_2), 31.7 (CH_2), 111.8 (CH), 117.5 (CH), 119.3 (CH), 121.0 (C), 122.4 (CH), 125.4 (C), 125.5 (CH), 126.3 (C), 127.3 (C), 127.7 (CH), 128.8 (CH), 129.7 (CH), 134.1 (C), 134.2 (C), 136.9 (C), 136.7 (C) ppm. IR spectrum (KBr): v = 3404, 3030, 2896, 2848, 1608 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{19}H_{14}NClNa$ $[M + Na]^+$ 314.0707; found 314.0706.

1-Bromo-2-methyl-3-nitrobenzene (16)[23]: Copper (II) sulfate (17.5 g, 70.0 mmol) and sodium bromide (8.0 g) was dissolved in water (60 mL) on warming in hot water bath. To this warm solution sodium dithionate (4.6 g) solution in water (40 mL) was added portion-wise with occasional shaking and warming in hot water bath. Afterwards solid sodium dithionate (1 g) was added in portion-wise to the reaction mixture and thereby the color of the solution was changed from greenish blue to yellowish grey. The supernatant aqueous part was decanted off to obtain solid mass of cuprous bromide to which conc. HBr (20.5 mL) and water (50 mL) were added and the resulting solution was allowed to cool in ice-water bath for 1 hr. In the mean time 2-methyl-3-nitroaniline (**15**, 7.7 g, 50.0 mmol) was suspended in water (65 mL) and then heated to reflux. To this boiling solution conc. HBr (26.0 mL) was added in drop-wise manner and refluxing was continued for further 20 min. This hot acid solution of 2-methyl-3-nitroaniline (**15**) was then allowed to cool to 0 °C in ice-water bath. To this solution cooled aq. solution of sodium nitrite (3.6 g in 18 mL water) was added in drop-wise manner maintaining reaction temperature below 0 °C using ice-acetone bath. This diazotization was completed in 20 min. Cooled diazotized solution was added in drop-wise manner to the cooled solution of CuBr-HBr under cold condition during 1 hr. with good stirring and stirring was continued for further 30 min. During this period the color of the solution was changed from reddish violet to yellowish green with the evolution of nitrogen gas which resulted in frothing. The reaction mixture was then heated on water bath for about 20 min. with occasional shaking. This was kept overnight at room temperature. The solid thus separated out was steam distilled and extracted with ether (500 mL). The ether layer was washed with brine and dried over anhydrous Na_2SO_4. After evaporation of ether under vacuum, white solid compound **16** (9.0 g, yield 84%) was obtained, m.p. 37 °C (ref.[23] 36-39 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.55(s, 3H, Ar-CH_3), 7.19 (q, 1H, Ar-H), 7.71 (dd, J = 0.9, 0.9 Hz, 1H, Ar-H), 7.78 (dd, J = 1.2, 1.2 Hz, 1H, Ar-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4 (CH_3), 123.2 (CH), 127.3 (CH), 127.5 (C), 132.4 (CH), 136.6 (C ×2) ppm. IR spectrum (KBr): v = 3452, 3434, 3082, 3004, 1595, 1529 cm^{-1}. HRMS (Q-TOF): calcd. for $C_7H_6BrNO_2H$ $[M + H]^+$ 215.9657; found 215.9660.

3-Bromo-2-methylaniline (17): To the methanol (50 mL) solution of 1-bromo-2-methyl-3-nitrobenzene (**16**, 5.4 g, 25.0 mmol), NH_4Cl solution (2.5 g in 100 mL water), iron powder (12.5 g) and charcoal (1.0 g) were added and the reaction mixture was heated under reflux for 4 hr. After cooling to room temperature the reaction mixture was filtered and the residue was washed with ether. Then the filtrate portion was extracted with ether (4 × 25 mL). Ether layer was washed with brine solution and

then dried over anhydrous Na_2SO_4. Evaporation of ether afforded 3-bromo-2-methylaniline (**17**, 4.3 g, yield 92%) as pale yellow oil,[30] b.p. 245 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3H, Ar-CH_3), 3.65 (s, 2H, NH_2), 6.60 (d, *J* = 7.2, 1H, Ar-H), 6.88 (t, 1H, Ar-H), 7.03 (d, *J* = 7.2 Hz, 1H, Ar-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.8 (CH_3), 114.0 (CH), 121.8 (CH), 122.6 (CH), 125.8 (C), 127.5 (C), 145.8 (C) ppm. IR spectrum (KBr): v = 3352, 3323, 2982, 2947, 1573 cm^{-1}. HRMS (Q-TOF): calcd. for C_7H_8BrNNa $[M + Na]^+$ 207.9734; found 207.9736.

3-Bromo-2-methylphenol (18): 3-Bromo-2-methylaniline (**17**, 6.3 g, 34.0 mmol) was taken in dilute H_2SO_4 solution (6.2 mL conc. H_2SO_4 in 30 mL water) and cooled to 0 °C in ice-salt bath. This was diazotized with aq. $NaNO_2$ solution (2.76 g, 40 mmol in 10 mL water) under cold condition maintaining reaction temperature around 0-5 °C during 45 min. After diazotization the reaction mixture was diluted with ice-water (60 mL) and treated with pinch of urea to remove excess nitrous acid. In the mean time mixture of anhydrous Na_2SO_4 (12.75 g), conc. H_2SO_4 (15.3 mL) and water (10 mL) was heated in oil bath at about 150 °C. To this hot solution cooled diazotized solution was added in portion-wise during half an hour and when the evolution of nitrogen was ceased the reaction mixture was heated under reflux for 1 hr. The reaction mixture was then allowed to cool at room temperature and extracted with ether (5×50mL). Ether extract was washed with brine solution (1×40mL) followed by water (1×40mL) and then dried over anhydrous Na_2SO_4. Evaporation of ether yielded low melting 3-bromo-2-methylphenol (**18**, 4.6 g, yield 73%) as needle like crystals of m.p. 97 °C (ref.[31] 95 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, Ar-CH_3), 4.41 (s, br, 1H, OH), 6.70 (d, *J* = 4.8, 1H, Ar-H), 6.90 (t, 1H, Ar-H), 7.13 (d, *J* = 4.8 Hz, 1H, Ar-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.15 (CH_3), 113.66 (CH), 124.14 (CH), 124.58 (C), 125.68 (CH), 127.04 (C), 153.93 (C) ppm. IR spectrum (KBr): v = 3288, 2923, 2854, 1579 cm^{-1}. HRMS (Q-TOF): calcd. for C_7H_7BrOH $[M + H]^+$ 186.9756; found 186.9759.

4-Amino-3-bromo-2-methylphenol (20): In 250 mL conical flask 5.25 g (30.0 mmol) of sulfanilic acid was suspended in 50 mL of water. It was then neutralized by using 1.6 g (15.0 mmol) of sodium carbonate in 50 mL of water. Resulted clear solution was cooled to 0 °C in ice-water bath. To this cold solution sodium nitrite solution (2.0 g, 30.0 mmol in 10 mL water) was added and this reaction mixture was then poured into ice-hydrochloric acid mixture (5.5 mL of conc. HCl and 30 g of ice) to obtain finely divided crystals of diazobenzene sulfonate. The aqueous suspension was then kept in freeze. In the mean time 3-bromo-2methylphenol (**18**, 5.6 g, 30.0 mmol in 20 mL 10% NaOH) was dissolved in aq, alkali and solution was cooled to 0-5 °C in ice-water bath. To this cold solution the aqueous suspension of diazobenzene sulfonate was added all at once with stirring. Colored dye with pasty mass appeared instantly. The whole reaction mixture was then kept in freeze for 30 min. The reaction mixture was then warmed on water bath to dissolve the pasty mass and then 25 g of sodium chloride was dissolved in the warm solution. To this warm alkaline solution solid sodium dithionate (25.0 g) was added in portions with stirring until the dark red color of the solution was discharged. The reaction mixture was then cooled in freeze. A solid mass was separated out which was collected through filtration and washed with very little amount of cold water to obtain 4-amino-3-bromo-2-methylphenol (**20**, 3.9 g, yield 66%) as light brown solid, m.p. 161 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.15 (s, 3H, Ar-CH_3), 4.79 (s, br, 1H, OH), 6.54 (d, *J* = 5.1, 1H, Ar-H), 6.60 (d, *J* = 5.1, 1H, Ar-H), 8.76 (s, 2H, NH_2) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 16.1 (CH_3), 112.3 (CH), 113.2 (CH), 114.8 (C), 123.6 (C), 137.9 (C), 146.7 (C) ppm. IR spectrum (KBr): v = 3350, 3261, 2923, 2804, 1604 cm^{-1}. HRMS (Q-TOF): calcd. for C_7H_8BrNOH $[M + H]^+$ 201.9864; found 201.9866.

4-Acetamido-3-bromo-2-methylphenol (21): To the warm (~60°C) aqueous suspension of 4-amino-3-bromo-2-methylphenol (**20**, 2.0 g, 10.0 mmol in 25.0 mL water), acetic anhydride (1.0 mL, 10.0 mmol) was added in all at once with stirring. The whole reaction mixture was kept on hot water bath for 1 hr. with occasional shaking. This was cooled to room temperature and then cooled in freeze overnight. The brownish solid thus formed was collected through filtration and then crystallized from water along with the charcoal treatment for purification to afford *N*-(2-bromo-4-hydroxy-3-methylphenyl)acetamide or 4-acetamido-3-bromo-2-methylphenol **(21,** 2.1 g, yield 89%**)** as white crystals**,** m.p. 159 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.97 (s, 3H, CH_3), 2.20 (s, 3H, Ar-CH_3), 6.76 (d, *J* = 5.1, 1H, Ar-H), 7.04 (d, *J* = 5.1 Hz, 1H, Ar-H), 9.25, (s, 1H, OH), 9.77 (s, 2H, NH_2) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ = 16.3 (CH_3), 23.0 (CH_3), 113.5 (CH), 123.6 (CH), 124.3 (C), 126.0 (C), 128.0 (C), 153.8 (C), 168.5 (C) ppm. IR spectrum (KBr): v = 3531, 3220, 3053, 2925, 1625 cm^{-1}. HRMS (Q-TOF): calcd. for $C_9H_{10}BrNO_2H$ $[M + H]^+$ 243.9969; found 243.9971.

***N*-(2-bromo-4-methoxy-3-methylphenyl)acetamide (22):** To the solution of *N*-(2-bromo-4-hydroxy-3-methylphenyl)acetamide (**21**, 2.4 g, 10.0 mmol) in acetone (25 mL) anhydrous potassium carbonate (1.38 g, 10.0 mmol) and iodomethane (0.6 mL, 10.0 mmol) were added. The reaction mixture was heated under reflux on hot water bath with circulation of ice cold water through condenser for 2 hr. Afterwards the reaction mixture was poured in ice-water (100 mL) whereby the required methoxy derivative **22** was separated out. This crude product was collected by filtration and leached with cold solution 1% NaOH (15 mL) followed by cold water. It was then crystallized from aqueous methanol to afford *N*-(2-bromo-4-methoxy-3-methylphenyl)acetamide (**22**, 2.4 g, yield 94%) as bright white crystals, m.p. 137 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3H, CH_3), 2.33 (s, 3H, Ar-CH_3), 3.81(s, 3H, -OCH_3), 6.80 (d, *J* = 5.4, 1H, Ar-H), 7.51 (s, 2H, NH_2), 7.98 (d, *J* = 5.1, 1H, Ar-H) ppm. ^{13}C NMR 75 MHz, $CDCl_3$): δ = 16.0 (CH_3), 24.2 (CH_3), 55.6 (CH_3), 109.0 (CH), 118.1 (CH), 120.1 (C), 126.7 (C), 128.4 (C), 154.3 (C), 167.8 (C) ppm. IR spectrum (KBr): v = 3267, 2925, 2844, 1652 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{10}H_{12}BrNO_2Na$ $[M + Na]^+$ 279.9944; found 279.9946.

2-Bromo-4-methoxy-3-methylbenzenaminium chloride (23): *N*-(2-bromo-4-methoxy-3-methylphenyl)acetamide (**22**, 2.5 g, 10.0 mmol) was dissolved in ethanol (15.0 mL) by boiling and concentrated HCl (15.0 mL) was added drop-wise under reflux during 1 hr. After 3 hr, the solution was cooled when the crystals of amine hydrochloride (**23**) separated out, which was collected by filtration to furnish colourless crystals (2.2 g, yield 86%), m.p. 218 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.24 (s, 3H, Ar-CH_3), 3.79 (s, 3H, -OCH_3), 7.05 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.07 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.50 (s, 2H, NH_2) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 16.00 (CH_3), 56.29 (-OCH_3), 110.34 (CH), 119.58 (CH), 121.93 (C), 124.87 (C), 127.38 (C), 156.44 (C) ppm..

2-(2-Bromo-4-methoxy-3-methylphenyl)hydrazono)cyclohexanone (26): 2-Hydroxymethylene-cyclohexanone[20] (**24**, 1.26 g,10.0 mmol) in methanol (10 mL) was added to an aqueous solution of sodium acetate (2.2 g, 15 mL of water). To this a solution of 2-bromo-4-methoxy-3-methylphenyldiazonium chloride (**25**, prepared from 2.52 g, 10.0 mmol of 2-bromo-4-methoxy-3-methylbenzenaminium chloride, **23**) was added under mechanical agitation and the stirring was continued for 4 hr. when red solid of **26** was obtained. Filtration and crystallization from methanol yielded red crystals of **26** (2.6 g, yield 82%), m.p. 127 °C. R_f = 0.7 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.76 (q, 4H, CH_2), 2.22 (s, 3H, Ar-CH_3), 2.48 (t, 2H, CH_2), 2.61 (t, 2H, CH_2), 3.84 (s, 3H, -OCH_3), 7.02 (d, *J* = 11.0, 1H, Ar-H), 7.43 (d, *J* = 11.5, 1H, Ar-H), 13.85 (s, 1H, NH) ppm. ^{13}C NMR (125 MHz, DMSO-d_6): δ = 16.0 (CH_3), 21.7 (CH_2), 22.8 × 2 (CH_2), 31.8 (CH_2), 56.3 (CH_3), 111.5 × 2 (CH), 112.5 (C), 126.3 (C), 134.0 (C), 134.6 (C), 153.3 (C), 197.5

(C=O) ppm. IR spectrum (KBr): v = 3467, 3006, 2939, 1660, 1625 cm^{-1}; HRMS (Q-TOF): calcd. for $C_{14}H_{17}BrN_2O_2Na$ $[M + Na]^+$ 347.0346; found 347.0349.

8-Bromo-6-methoxy-7-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (12): 2-(2-Bromo-4-methoxy-3-methylphenyl)hydrazono)cyclohexanone (**26**, 1.6 g, 5.0 mmol) was heated under reflux with glacial acetic acid (12.8 mL) containing concentrated HCl (3.2 mL) for 3 min. and the hot reaction mixture was poured in ice water (50.0 mL). The semi-solid mass thus obtained was collected by filtration, washed with water, dried, and then chromatographed over silica gel (10 g) and the column was eluted with hexane–dichloromethane (3:2). The eluent gave colourless crystals of **12** (1.2 g, yield 78%), m.p. 212 °C (dec.). R_f = 0.5 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.26 (q, 2H, CH_2), 2.47 (s, 3H, Ar-CH_3), 2.63-2.69 (m, 2H, CH_2), 3.04 (t, 2H, CH_2), 3.97 (s, 3H, -OCH_3), 7.26 (s, 1H, Ar-H), 11.38 (s, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 16.1 (CH_3), 21.0 (CH_2), 24.5 (CH_2), 38.3 (CH_2), 56.0 (CH_3), 99.7 (CH), 108.0 (C), 123.9 (C), 126.3 (C), 128.8 (C), 131.6 (C), 132.4 (C), 152.4 (C), 189.8 (C) ppm. IR spectrum (KBr): v = 3288, 3261, 2945, 2914, 1666, 1642 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{14}H_{14}BrNO_2Na$ $[M + Na]^+$ 330.0100; found 330.0102.

1-Bromo-3-methoxy-2-methyl-9*H*-carbazole (11): Compound **12** (1.5 g, 5.0 mmol) in ethylene glycol (10 mL) was heated with hydrazine hydrate (80%, 4.5mL) and KOH (1.7g) at 190 °C for 1 hr. and then up to 210 °C under reflux for 3 hr. The reaction mixture was poured into ice-water and then extracted with diethyl ether (3 × 75 mL). The combined ether layers were dried (Na_2SO_4) and the solvent was distilled off, when a residue (1.4 g) of the corresponding tetrahydrocarbazole derivative was obtained. The residue was used for the next step without further purification. Crude tetrahydrocarbazole derivative (1.4 g) was taken in decalin (10 mL) and then Pd-C (l0%, 500 mg) added. The mixture was then refluxed for 5 hr. After reaction, decalin was removed by distillation under vacuum. The residue was subjected to flash chromatography on silica gel G and eluted with hexane to afford 3-methoxy-2-methyl-9*H*-carbazole (**27**) (120.0 mg, yield 11%) and with hexane-dichloromethane (9:1) to furnish 1-bromo-3-methoxy-2-methyl-9*H*-carbazole[32] (**11**, 950 mg, yield 65%), m.p. 168 °C. R_f = 0.8 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (s, 3H, CH_3) 3.95 (s, 3H, -OCH_3), 7.21 - 7.26 (m, 1H, Ar-H), 7.39 - 7.46 (m, 3H, Ar-H), 7.99 (d, J = 6.0 Hz, 1H, Ar-H) 8.07 (s, 1H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.0 (CH_3), 56.7 (CH_3), 100.8 (CH), 107.4 (C), 111.1 (CH), 119.6 (C), 120.4 (CH), 121.3 (CH), 124.1 (C), 125.5 (C), 125.8 (CH), 133.6 (C), 139.4 (C), 152.7 (C) ppm. IR spectrum (KBr): v = 3384, 2952, 2924, 1608, 1588 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{14}H_{12}BrNOH$ $[M + H]^+$ 290.0176; found 290.0174.

Hyellazole (1): 1-Bromo-3-methoxy-2-methyl-9*H*-carbazole (**11**, 725.0 mg, 2.5 mmol) and tetrakis(triphenylphosphine)-palladium (0) (50.0 mg, 0.044 mmol) were stirred in 1,2-dimethoxyethane (25 mL) for 30 min. A solution of phenylboronic acid (312.0 mg,, 2.55 mmol) and potassium carbonate (345.0 mg, 2.5 mmol) in water (10 mL) was added to it and the mixture was refluxed for 72 hr. The solvent was then removed by evaporation and the residue was extracted with dichloromethane. The organic layer was washed with brine solution and the dried over anhydrous sodium sulfate. After evaporation of dichloromethane the residue was subjected to flash chromatography on silica gel G with hexane-dichloromethane (9:1) to afford 3-methoxy-2-methyl-1-phenyl-9*H*-carbazole, Hyellazole (**1**) as a white solid (510.0 mg, 71% yield), m.p. 134 °C (ref.[14] 132-134 °C). R_f = 0.8 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (s, 3H, CH_3) 3.95 (s, 3H, -OCH_3), 6.59 (d, J = 8.4 Hz, 1H, Ar-H), 6.90 – 7.14 (m, 2H, Ar-H), 7.21-7.30 (m, 2H, Ar-H), 7.36 (d, J = 9.0 Hz, 1H, Ar-H), 7.47-7.63 (m, 3H, Ar-H), 7.69-7.72 (m, 1H, Ar-H), 7.98 (s, br, 1H, NH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.6 (CH_3), 56.3 (CH_3), 110.6 (CH), 107.4 (CH), 111.1 (CH), 119.6 (CH), 120.4 (C), 121.3 (CH), 124.1 (C), 125.5 (C), 125.8 (C), 133.6 (C), 139.4 (C), 152.7 (C) ppm. IR spectrum (KBr): v = 3410, 2932, 1632 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{20}H_{17}NONa$ $[M + Na]^+$ 310.1202; found 310.1204.

Deoxycarbazomycin B (1A): Similar Suzuki cross-coupling reaction over 1-Bromo-3-methoxy-2-methyl-9*H*-carbazole (**11**, 290.0 mg, 1.0 mmol) with methylboronic acid (70.0 mg, 1.2 mmol) and tetrakis(triphenylphosphine)-palladium (0) (25.0 mg, 0.022 mmol) for 60 hr. yielded 3-methoxy-1,2-dimethyl-9*H*-carbazole, 4-deoxycarbazomycin B (**1A**) as a white solid (126.0 mg, 56% yield), m.p. 131 °C (ref.[20a] 129 - 130 °C). R_f = 0.7 (benzene/chloroform/diethylamine, 14:5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.45 (s, 3H, Ar-CH_3), 2.52 (s, 3H, Ar-CH_3), 3.94 (s, 3H, -OCH_3), 7.18 (d, J = 7.5 Hz, 1H, Ar-H), 7.25-7.32 (m, 2H, Ar-H), 7.36 (s, 1H, Ar-H), 7.66 (s, 1H, NH), 7.80 (d, J = 8.5 Hz, 1H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.3 (CH_3), 13.8 (CH_3), 56.3 (OCH_3), 99.0 (CH), 110.4 (CH), 119.0 (C), 119.8 (CH), 120.1 (C), 124.0 (CH), 124.3 (C), 126.3 (CH), 128.2 (C), 134.5 (C), 137.9 (C), 152.5 (C) ppm. IR spectrum (KBr): v = 3428, 2944, 1640 cm^{-1}. HRMS (Q-TOF): calcd. for $C_{15}H_{15}NONa$ $[M + Na]^+$ 248.1051; found 248.1054.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra for all key intermediates.

Acknowledgements

The author (S.C.) is grateful to Dr. Samir kanti Dutta (Vice Principle, Science) of The Bhawanipur Education Society College, Kolkata for his interest and support in this work and the laboratory provided by the college. The authors are also thankful to the Department of Clinical & Experimental Pharmacology of the School of Tropical Medicine, Kolkata.

Keywords: marine alkaloid• natural product • Suzuki-Miyaura cross-coupling • hyellazole • 4-deoxycarbazomycin B • total synthesis

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