2-Acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one in the synthesis of heteroannulated carbazoles

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The reaction of 2,3,4,9-tetrahydro-1*H*-carbazol-1-ones with ethyl acetate yielded 2-acetyl-1-hydroxycarbazole and 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one. These were used to prepare isoxazolo- and pyrazolo-fused carbazoles. Mechanisms for the formation of the end products are proposed.

Keywords: fused carbazoles, isoxazoles, pyrazoles, indazoles

Carbazoles are structural subunits found in numerous naturally occurring compounds as well as synthetic materials, and many of them display high pharmacological activity.[1] For example, ellipticine and its analogs in particular have been found to possess promising antitumor[2-8] and anti-HIV[9] activities, which prompted numerous studies into the structure-activity relationships of heteroannulated carbazoles. Efforts have also been invested in developing efficient synthetic avenues to heteroannulated carbazoles and their structurally modified derivatives, and these are well documented.[3,10] As synthetic materials, many carbazoles exhibit photo-reactive, photoconductive and light emitting properties.[11,12] Carbazole has also been recognised as a useful scaffold in anion binding studies.[13] Consequently the syntheses of carbazoles and their characterisation have been a vigorously active area of study.

In our present work, we planned to prepare functionalised carbazoles from 2,3,4,9-tetrahydro-1*H*-carbazol-1-ones and to elucidate the structures of the newly prepared fused systems.

Results and discussion

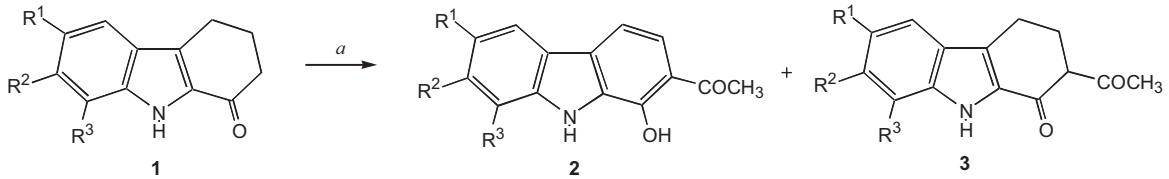
When 8-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**1a**) reacted with ethyl acetate in the presence of sodium hydride and a catalytic amount of potassium hydride as co-reactant, a brown semisolid mass was formed which on separation by column chromatography on silica gel using petroleum ether/ethyl acetate as eluant afforded three products. The first, obtained from the petroleum ether fraction, was simply ethyl acetoacetate. The second fraction, a yellow powder (yield 10%), eluted by petroleum ether/ethyl acetate (98 : 2), melted at 180–182°C, and proved to be the known 2-acetyl-1-hydroxy-8-methylcarbazole (**2a**) (mixed m.p., superimposable IR spectra).[14]

The third product, which was the major component (yield 75%), was obtained from the petroleum ether/ethyl acetate (95 : 5) fraction as a yellow powder, m.p. 129–131°C. Its IR spectrum showed NH stretching at 3308 cm^{-1} and carbonyl bands appeared at 1710 and 1637 cm^{-1}. The ^1H NMR spectrum exhibited a singlet at δ 15.48 for the enolic OH at C1, a one proton broad singlet at δ 8.78 for N9-H, a three proton multiplet between δ 7.29 and 7.04 for C5, C6 and C7 aromatic protons. The aliphatic protons appeared as one proton multiplet between δ 3.74 and 3.67 for C2, two multiplets each for two protons centred at δ 3.00 and 2.65 for C4-H_2 and C3-H_2 respectively, two three-proton singlets at δ 2.49 and 2.35 were assigned to C8-CH_3 and C2-$COCH_3$ respectively. The mass spectrum exhibited the molecular ion peak at *m/z* 241 (43%). The elemental analysis agreed well with the proposed molecular formula $C_{15}H_{15}NO_2$. All the spectral and analytical results were consistent with the product being 2-acetyl-8-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3a**), with the 1-OH enol form a minor tautomeric component. The reaction was performed with other carbazole derivatives **1b–e** in order to realise the respective 2-acetyl-1-hydroxycarbazoles **2b–e** and 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-ones **3b–e** (Scheme 1).

It should be noted that the use of potassium hydride as co-reactant proved necessary for the formation of the products. The same reaction without the addition of potassium hydride or using other bases like NaOMe, NaOEt, alc.KOH, pyridine-KOH did not yield the desired products **2** and **3**. The 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**) enolised and this on further aerial oxidation produced the fully aromatised 2-acetyl-1-hydroxy carbazole (**2**). To avoid the concurrent formation of ethyl acetoacetate, we first carried out the reaction of 2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**1**) with ethyl acetate in equimolar ratio. However, the reaction was incomplete and ethyl acetoacetate was still obtained. Therefore we employed an excess of ethyl acetate in the reaction.

In order to achieve the synthesis of heteroannulated carbazoles, we treated the 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-ones (**3**) with hydroxylamine hydrochloride, hydrazine hydrate and semicarbazide hydrochloride.

The reaction of 2-acetyl-8-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3a**) with hydroxylamine hydrochloride in glacial acetic acid yielded colourless needles which melted at 198–200°C. Its IR spectrum showed NH stretching at 3372



Scheme 1

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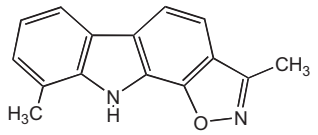
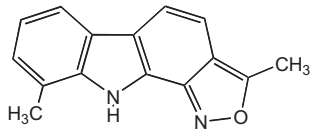
cm^{-1}. The ^1H NMR spectrum in $CDCl_3$ exhibited a one proton broad singlet at δ 8.63 due to N10-H, a two proton multiplet between δ 8.03 and 7.89 was due to C5- and C6- protons, a one proton doublet (J = 8.20 Hz) at δ 7.45–7.41 was due to C4-H, a two proton multiplet at δ 7.34–7.20 for C7- and C8-H. Two three-proron singlets at δ 2.68 and δ 2.66 were due to C3-and C9-CH_3 respectively. The absence of aliphatic protons for C3- and C4-H_2 indicated that the resulted product was fully aromatised. The ^{13}C NMR spectrum also showed the presence of 15 nonequivalent carbons, and the elemental analysis was in agreement with the molecular formula $C_{15}H_{12}N_2O$. The mass spectrum showed the molecular ion peak at *m/z* 236.

Since the starting material **3a** contained two keto groups and the reaction had taken place at these sites, the spectral and analytical results suggested the structure of the product to be either 3,9-dimethyl-10*H*-isoxazolo[5,4-*a*]carbazole (**4a**) or 3,9-dimethyl-10*H*-isoxazolo[3,4-*a*]carbazole (**4a'**).



4a



4a'

A distinction between these structures was achieved as follows:

(i) Support for structure **4a** was obtained from MM2 energy calculations. The steric energy was calculated for both structures, and that for **4a** was found to be 24.9145 kcal/mol whereas for **4a'** it was found to be 25.1349 kcal/mol. The lower energy structure **4a** was preferred over the higher energy structure **4a'**.

(ii) X-ray crystallographic studies[15] confirmed the structure to be **4a**. The bond lengths of C3a–C10b (1.364 Å) and C3–C3a (1.420 Å) suggested that an aromatic double bond was at C3a–C10b (for a pure double bond 1.34 Å is expected) and this strongly supported the structure of the product as 3,9-dimethyl-10*H*-isoxazolo[5,4-*a*]carbazole (**4a**). The X-ray crystal structure is shown in Fig. 1.

From all the above facts, we assigned the structure of the product as 3,9-dimethyl-10*H*-isoxazolo[5,4-*a*]carbazole (**4a**). This reaction was generalised for other carbazole derivatives (**1b–e**) to form the respective 3-methyl-10*H*-isoxazolo[5,4-*a*] carbazoles (**4b–e**) (Scheme 2).

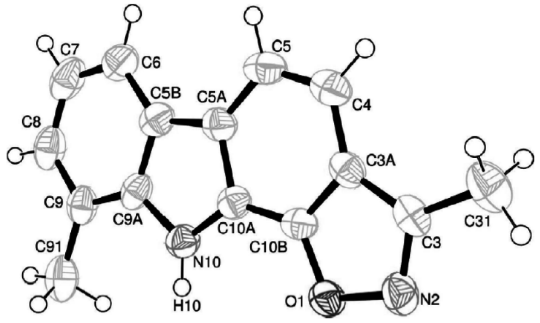


Fig. 1 Crystal structure of 3,9-dimethyl-10*H*-isoxazolo[5,4-*a*] carbazole (**4a**).

The reaction of 2-acetyl-8-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3a**) with hydrazine hydrate in glacial acetic acid yielded a mixture of two products. The products were separated by column chromatography over silica gel using petroleum ether/ethyl acetate as eluant. The major product (yield 75%) obtained from the petroleum ether/ethyl acetate (98 : 2) fraction melted at 142–144°C; Its IR spectrum exhibited NH stretching at 3275 cm^{-1}. The C=N stretching appeared at 1630 cm^{-1}. Its ^1H NMR spectrum in $CDCl_3$ exhibited two broad singlets at δ 12.00 and 11.12 for N1-H and N10-H; four doublets in the aromatic region for C6, C5, C4 and C8-H respectively and a further one-proton multiplet at δ 7.07–7.01 for C7–H, and two singlets at δ 2.55 and 2.49 for C9–CH_3 and C3–CH_3 respectively. The molecular ion peak appeared at *m/z* 235.

Similar to the previous case, this product was also a fully aromatised compound. Conclusive evidence for structure **5a** was obtained from an X-ray crystallographic study (Fig. 2).[16] The product was thus identified as 1,10-dihydro-3,9-dimethyl pyrazolo[3,4-*a*]carbazole (**5a**).

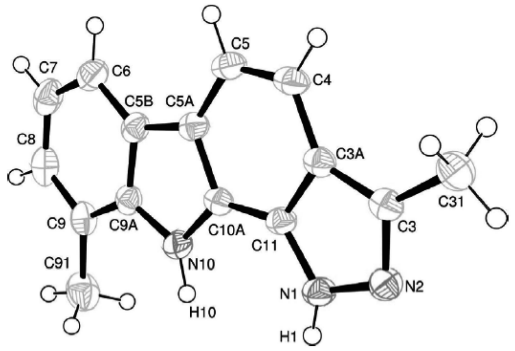
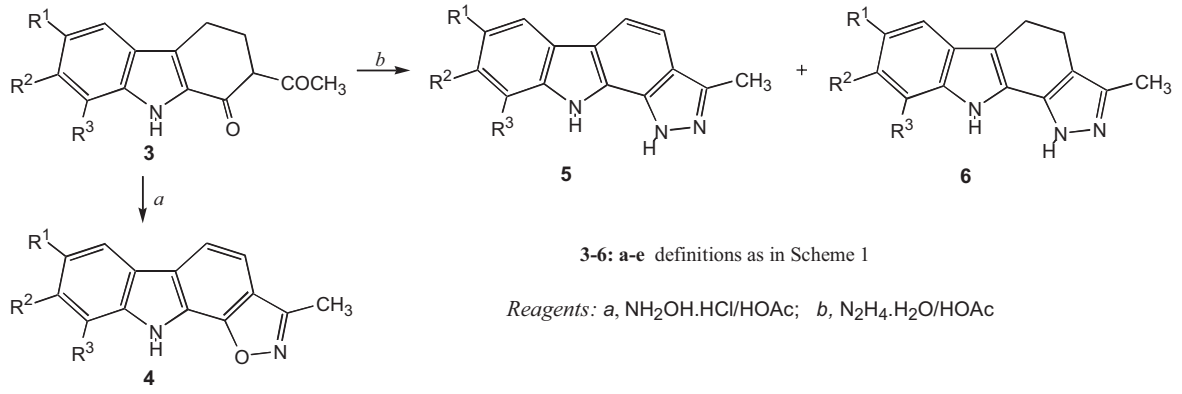


Fig. 2 Crystal structure of 1,10-dihydro-3,9-dimethylpyrazolo [3,4-*a*]carbazole (**5a**).



3-6: a-e definitions as in Scheme 1

Reagents: a, $NH_2OH.HCl/HOAc$; *b*, $N_2H_4.H_2O/HOAc$

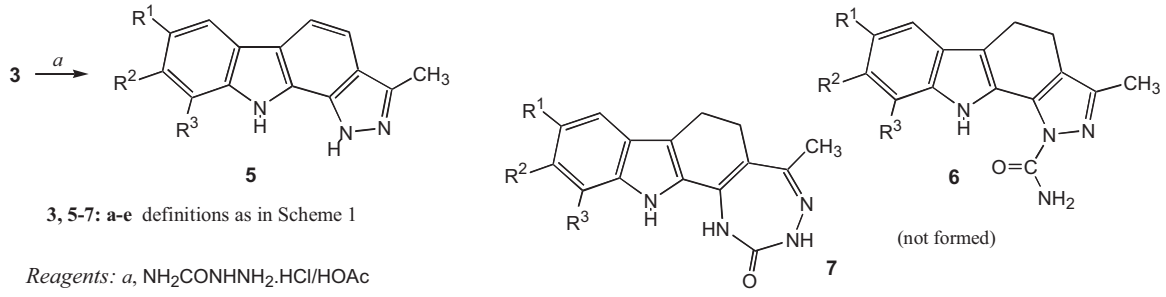
Scheme 2

The minor product (yield 15%) obtained from the petroleum ether/ethyl acetate (95.5) fraction melted at 168–170°C. Its IR spectrum showed the absence of a free carbonyl group, clearly indicating a cyclised product. The ^{1}H NMR spectrum in $CDCl_3$ showed two broad singlets each for one proton at δ 12.05 and 11.13 for N1- and N10-protons respectively, a one proton doublet at δ 7.90–7.82 for C6-H and a multiplet at δ 7.19–7.01 for two protons corresponding to C7 and C8–H in the aromatic region. Two more multiplets at δ 3.00–2.89 and 2.82–2.70 each for two protons were assigned to methylene protons at C5 and C4 respectively, and two three-proton singlets at δ 2.57 and 2.23 corresponding to C9–CH_3 and C3–CH_3 groups respectively. The elemental analysis showed the molecular formula as $C_{15}H_{15}N_3$. The mass spectrum showed the molecular ion peak at *m/z* 237. All the spectral and analytical results thus supported the structure as 1,4,5,10-tetrahydro-3,9-dimethylpyrazolo[3,4-*a*]carbazole (**6a**) (Scheme 2).

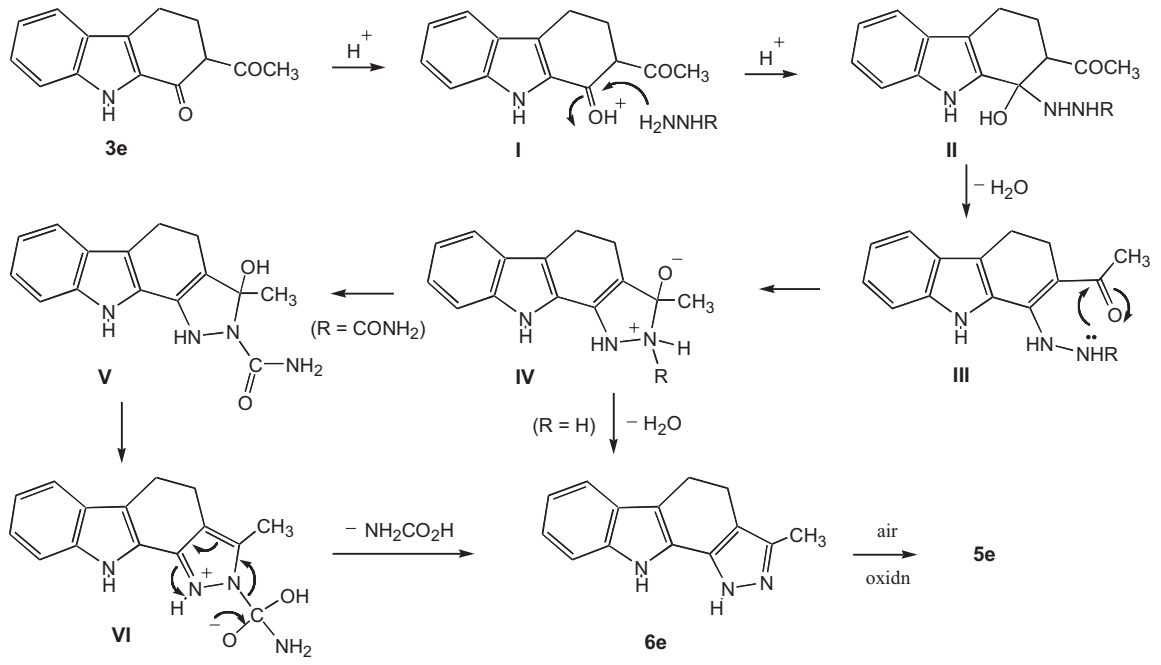
It should be noted that, on keeping this tetrahydro compound for a week in the open air, it was slowly oxidised to **5a**. The generality was tested with other carbazole derivatives, **1b–e**. (Scheme 2)

Our earlier work on methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetate[19] with semicarbazide hydrochloride prompted us to apply similar reaction conditions to 2-acetyl-8-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3a**). This reaction resulted in the exclusive formation of 1,10-dihydro-3,9-dimethylpyrazolo[3,4-*a*]carbazole (**5a**) as product, which was one of the products of the reaction of **3a** with hydrazine hydrate. The tetrahydro product, **6a**, was not realised in this case. Also we did not observe other possible products such as 4,6,7,12-tetrahydro-5,9-dimethyl[1,2,4]triazepino[5,6-*a*]carbazol-2(1*H*)-one(**7**)and/or4,5-dihydro-3,7-dimethylpyrazolo[3,4-*a*]carbazole-1(10*H*)-carboxamide (**8**). The product **5a** was confirmed by mixed m..p., superimposable IR, ^{1}H NMR and mass spectra. The generality was tested with the other 2-acetyltetrahydrocarbazolone derivatives **3b–e** (Scheme 3).

A mechanistic rationalisation for the formation of **5** from the reaction of **3** with hydrazine hydrate as well as with semicarbazide hydrochloride is given in Scheme 4 (for simplicity, exemplified in the **e** series). The initial event is formation of the protonated intermediate **I** in presence of an acid catalyst.The nucleophile, NH_2NHR (R = H, $CONH_2$), can then add to the carbon of the hydroxycarbenium (oxonium) ion **I** to give the tetrahedral intermediate **II**, which loses a water molecule and a proton to give the intermediate **III**. This intermediate thus formed can, in principle, cyclise by the intramolecular nucleophilic attack of the amino group of the hydrazine part to give a five-membered 1,3-pyrazoline zwitterion derivative **IV**. If R = H, then the 1,3-pyrazoline derivative formed on prototropic shift and water elimination to give the dihydro product (**6**). Otherwise, if R = $CONH_2$ then the zwitterion **IV** on losing the elements of CO_2 and NH_3 gives the dihydro product, **6**. Finally **6** on aerial oxidation produced the fully aromatised product **5** as shown in Scheme 4.



Scheme 3



Scheme 4

Our results show that an important precursor, 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one, for the construction of some heteroannulated carbazoles can conveniently be prepared. It was successfully utilised for the syntheses of heteroannulated carbazoles like 1,10-dihydro-3-methyl-pyrazolo[3,4-*a*]carbazoles and 3-methyl-10*H*-isoxazolo[5,4-*a*]carbazoles.

Experimental

Melting points were determined using a Mettler FP 51 apparatus (Mettler Instruments, Switzerland). IR spectra were recorded in KBr on a Shimadzu FTIR-8201PC spectrophotometer (Shimadzu, Japan). ^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian AMX 400 FT-NMR (Varian, Australia) using TMS as internal standard. Mass spectra were recorded on a Jeol JMS-D-300 mass spectrometer (70 eV) (Jeol, Japan). Micro analyses were done on a Vario EL III Model CHNS analyser (Vario, Germany). The purity of the products was tested by TLC using glass plates coated with silica gel G (Hi Media Laboratories, India) and petroleum ether: ethyl acetate (90: 10) as the developing solvents. Ethyl acetate and sodium hydride (60% suspension in mineral oil) were obtained from LOBA Chemie Pvt. Ltd., India, and potassium hydride (30% suspension in mineral oil) from Aldrich.

Reaction of 2,3,4,9-tetrahydro-1H-carbazol-1-ones (**1a-e**) *with ethyl acetate: General procedure*

2,3,4,9-Tetrahydro-1*H*-carbazol-1-one **1** (8 mmol) was added to sodium hydride (2.4 g) suspended in benzene (20 ml) in a two necked round-bottomed flask fitted with reflux condenser and calcium chloride guard tube, and heated on a water bath for 5 minutes. Then potassium hydride was added carefully (*Caution*: dry potassium hydride is highly pyrophoric). It was heated to reflux for 2 minutes. To this ethyl acetate was added dropwise from a dropping funnel. After the addition was complete reflux was continued for 2 h. The solution became red. After cooling in an ice bath the solution was cautiously neutralised with acetic acid. Some further acetic acid was added and then the whole was poured into ice water and extracted using ethyl acetate. The extract was washed thoroughly with water and brine, then dried (Na_2SO_4). Filtration and solvent removal *in vacuo* left a crude mass which was purified by column chromatography over silica gel using petroleum ether/ethyl acetate mixtures (100 : 0; 98 : 2 and 95 : 5) as eluant. The petroleum ether fraction yielded ethyl acetoacetate. The petroleum ether/ethyl acetate (98 : 2) fraction yielded 2-acetyl-1-hydroxycarbazole (**2**). The petroleum ether/ethyl acetate (95 : 5) fraction yielded 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**).

2-Acetyl-8-methylcarbazol-1-ol (**2a**): Yellow crystalline powder (10%, EtOH), m.p. 177–178°C.

2-Acetyl-8-methyl-2,3,4,9-tetrahydro-1H-carbazol-1-one (**3a**): Yellow powder (56%); m.p. 129–131°C. IR: ν_{max} 3308, 2926, 1710, 1637, 1542 cm^{-1}. NMR: δ_H 15.48 (s, C1 enolic OH), 8.78 (br s, 1H, N9-H), 7.29–7.04 (m, 3H, C5, C6, C7-H), 3.74–3.67 (m, 1H, C2-H), 3.06–2.93 (m, 2H, C4-H_2), 2.70–2.59 (m, 2H, C3-H_2), 2.49 (s, 3H, C8-CH_3), 2.35 (s, 3H, C2-$COCH_3$); δ_C 200.2 (C2-$\underline{C}OCH_3$), 190.5 (C1), 134.3, 133.6, 129.4, 128.4, 126.4, 119.7, 118.6, 112.3 (eight aromatic C), 56.7 (C2), 28.5 (C2-CO$\underline{C}H_3$), 25.7 (C8-CH_3), 24.8 (C3), 22.6 (C4). MS: *m/z* (%) 241 (43). Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81; Found: C, 74.79; H, 6.18; N, 5.84%.

2-Acetyl-7-methylcarbazol-1-ol (**2b**): Yellow powder (12%, EtOH), m.p. 146–148°C.

2-Acetyl-7-methyl-2,3,4,9-tetrahydro-1H-carbazol-1-one (**3b**): Yellow powder (50%), m.p. 137–139°C. IR: ν_{max} 3270, 2929, 1718, 1650, 1592 cm^{-1}. NMR: δ_H 15.50 (s, C1-enolic OH), 8.70 (br s, 1H, N9-H); 7.30–7.14 (m, 3H, C5, C6, C8-H); 3.71–3.64 (m, 1H, C2-H), 3.30–3.13 (m, 2H, C4-H_2), 3.06–2.94 (m, 2H, C3-H_2), 2.65 (s, 3H, C7-CH_3), 2.34 (s, 3H, C2-$COCH_3$); δ_C 202.3 (C2-$\underline{C}OCH_3$), 194.7 (C1), 138.4, 134.2, 130.1, 128.9, 127.6, 120.1, 118.1, 111.4 (eight aromatic C), 60.1 (C2), 29.3 (C2-CO$\underline{C}H_3$), 27.5 (C7-CH_3), 24.1 (C3), 20.7 (C4). MS: *m/z* (%) 241 (34). Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81; Found: C, 74.37; H, 6.20; N, 5.81%.

2-Acetyl-6-methylcarbazol-1-ol (**2c**): Pale yellow powder (10%, EtOH), m.p. 170–172°C.

2-Acetyl-6-methyl-2,3,4,9-tetrahydro-1H-carbazol-1-one (**3c**): Yellow powder (54%), m.p. 125–127°C. IR: ν_{max}, KBr, 3278, 2926, 1716, 1640, 1582 cm^{-1}. NMR: δ_H 15.48 (s, C1-enolic OH), 8.92 (br s, 1H, N9-H), 7.48–7.15 (m, 3 H, C5, C7, C8-H); 3.73–3.66 (m, 1H, C2-H), 3.08–2.94 (m, 2H, C4-H_2), 2.86–2.78 (m, 2H, C3-H_2), 2.45 (s, 3H, C6-CH_3), 2.15 (s, 3H, C2-$COCH_3$); δ_C 203.0 (C2-$\underline{C}OCH_3$), 189.9 (C1), 138.6, 135.0, 129.7, 128.9, 127.3, 119.8, 117.2, 109.5 (eight aromatic C), 62.3 (C2), 29.3 (C2-CO$\underline{C}H_3$), 28.4 (C6-CH_3), 25.3 (C3), 19.7 (C4). MS: *m/z* (%) 241 (38). Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81; Found: C, 74.29; H, 6.18; N, 5.87%.

2-Acetyl-6-chlorocarbazol-1-ol (**2d**): Yellow powder (15%, EtOH), m.p. 204–206°C. IR: ν_{max} 3403, 3259, 2924, 1693 cm^{-1}. NMR: δ_H 13.08 (s, 1H, C1-OH), 8.43 (br s, 1H, N9-H), 7.96–7.91 (d, 1H, C4-H, *J* = 8.00 Hz), 7.58–7.48 (m, 2H, C7, C8-H), 7.30 (s, 1H, C5-H), 7.12–7.08 (d, 1H, C3-H, *J* = 8.20 Hz), 2.54 (s, 3H, C2-$COCH_3$). MS: *m/z* (%) 259 (16). Anal. Calcd. for $C_{14}H_{10}ClNO_2$: C, 64.75; H, 3.88; N, 5.39; Found: C, 64.50; H, 3.92; N, 5.44%.

2-Acetyl-6-chloro-2,3,4,9-tetrahydro-1H-carbazol-1-one (**3d**): Yellow powder (48%), m.p. 141–143°C. IR: ν_{max} 3308, 2926, 1710, 1637, 1542 cm^{-1}. NMR: δ_H 15.43 (s, C1-enolic OH), 9.16 (br s, 1H, N9-H), 7.40–7.23 (m, 3 H, C5, C6, C7-H), 3.76–3.70 (m, 1H, C2-H), 3.00–2.90 (m, 2H, C4-H_2), 2.84–2.77 (m, 2H, C3-H_2), 2.18 (s, 3H, C2-$COCH_3$). δ_C 199.8 (C2-$\underline{C}OCH_3$), 192.0 (C1), 139.4, 134.6, 129.8, 127.6, 126.4, 120.8, 118.9, 112.3 (eight aromatic C), 64.3 (C2), 29.7 (C2-CO$\underline{C}H_3$), 26.1 (C3), 20.0 (C4). MS: *m/z* (%) 261 (24). Anal. Calcd. for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35; Found: C, 64.48; H, 4.57; N, 5.30%.

2-Acetylcarbazol-1-ol (**2e**): Pale yellow crystalline powder (20%; EtOH), m.p. 180–182°C.

2-Acetyl-2,3,4,9-tetrahydro-1H-carbazol-1-one (**3e**): Yellow powder (54%), m.p. 125–127°C. IR: ν_{max} 3270, 2920, 1709, 1643, 1578 cm^{-1}. NMR: δ_H 15.49 (s, C1-enolic OH), 8.78 (br s, 1H, N9-H), 7.44–7.11 (m, 4H, C5, C6, C7, C8-H), 3.05–2.94 (m, 2H, C4-H_2), 2.86–2.78 (m, 2H, C3-H_2), 2.36 (s, 3H, C2-$COCH_3$); δ_C 200.1 (C2-$\underline{C}OCH_3$), 191.7 (C1), 140.4, 136.7, 130.2, 124.7, 124.2, 120.6, 118.2, 112.9 (eight aromatic C), 64.4 (C2), 28.9 (C2-CO$\underline{C}H_3$), 24.3 (C3), 22.7 (C4). MS: *m/z* (%) 227 (33). Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16; Found: C, 74.09; H, 5.81; N, 6.14%.

Preparation of 3-methyl-10H-isoxazolo[5,4-a]carbazoles (**4a–e**): *General procedure*

To the appropriate 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**, 1 mmol) in glacial acetic acid (15 ml) was added hydroxylamine hydrochloride (10 mmol) and the solution was refluxed on an oil bath for 4 h. The reaction was monitored by TLC. After the completion of the reaction it was poured onto crushed ice. The precipitate was filtered off, washed with water and dried. It was purified by column chromatography over silica gel using petroleum ether: ethyl acetate (85 : 15) as eluant.

3,9-Dimethyl-10H-isoxazolo[5,4-a]carbazole (**4a**): Colourless needles (60%), m.p. 198–200°C. IR: ν_{max} 3372, 2920, 1657, 1565, 1445, 1386 cm^{-1}. NMR: δ_H 8.63 (br s, 1H, N10-H), 8.03–7.89 (m, 2H, C5, C6-H), 7.45–7.41 (d, 1H, C4-H, *J* = 8.20 Hz), 7.34–7.20 (m, 2H, C7, C8-H), 2.68 (s, 3H, C3-CH_3), 2.66 (s, 3 H, C9-CH_3); δ_C 156.3, 149.3, 134.7, 132.3, 128.3, 126.4, 124.3, 120.1, 118.7, 115.7, 112.3, 108.3, 104.3 (13 aromatic C), 21.4 (C9-CH_3), 19.6 (C3-CH_3) MS: *m/z* (%) 236 (28). Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86; Found: C, 76.20; H, 5.15; N, 11.87%.

3,8-Dimethyl-10H-isoxazolo[5,4-a]carbazole (**4b**): White amorphous powder (52%), m.p. 210–212°C. IR: ν_{max}, KBr, 3384, 2919, 1651, 1570, 1453 cm^{-1}. NMR: δ_H 8.60 (br s, 1H, N10-H), 8.03–7.90 (m, 2H, C5, C9-H), 7.45–7.35 (m, 3H, C4, C6, C7-H), 2.68 (s, 3H, C3-CH_3), 2.57 (s, 3 H, C8-CH_3); δ_C 157.6, 117.1, 135.6, 133.4, 127.9, 127.1, 125.1, 119.6, 116.8, 116.1, 115.2, 110.3, 109.1 (13 aromatic C), 20.7 (C8-CH_3), 20.1 (C3-CH_3). MS: *m/z* (%) 236 (22). Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86; Found: C, 75.98; H, 5.07; N, 11.89%.

3,7-Dimethyl-10H-isoxazolo[5,4-a]carbazole (**4c**): Colourless needles (65%), m.p. 225–227°C. IR: ν_{max} 3409, 2921, 1649, 1580, 1455 cm^{-1}. NMR: δ_H 8.61 (br s, 1H, N10-H), 7.98 (s, 1H, C6-H), 7.97–7.92 (d, 1H, C5-H, *J* = 8.00 Hz), 7.50–7.46 (d, 1H, C9-H, *J* = 8.26 Hz), 7.41–7.37 (d, 1H, C8-H, *J* = 8.26 Hz), 7.35–7.31 (d, 1H, C4-H, *J* = 8.00 Hz), 2.67 (s, 3H, C3-CH_3), 2.56 (s, 3 H, C7-CH_3); δ_C 152.4, 146.7, 135.3, 133.8, 129.1, 124.1, 122.1, 121.0, 114.8, 111.7, 110.3, 107.9, 108.7 (13 aromatic C), 24.0 (C6-CH_3), 22.5 (C3-CH_3). MS: *m/z* (%) 236 (30). Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86; Found: C, 76.67; H, 5.10; N, 11.81%.

7-Chloro-3-methyl-10H-isoxazolo[5,4-a]carbazole (**4d**): White powder (58%), m.p. 187–189°C. IR: ν_{max} 3427, 2925, 1652, 1580, 1460, 1435 cm^{-1}. NMR: δ_H 8.73 (br s, 1H, N10-H), 8.10 (s,1H, C6-H), 7.97–7.93 (d, 1H, C5-H, *J* = 8.00 Hz), 7.55–7.42 (m, 3H, C4, C7, C8-H), (s, 3H, C3-CH_3); δ_C 154.9, 146.1, 132.8, 130.3, 129.0, 127.4, 126.9, 122.6, 114.7, 111.7, 110.0, 108.7, 107.1 (13 aromatic C), 21.7 (C3-CH_3). MS: *m/z* (%) 256 (28). Anal. Calcd. for $C_{14}H_9N_2ClO$:

C, 65.51; H, 3.53; N, 10.91; Found: C, 65.60; H, 3.47; N, 10.85%.

3-Methyl-10H-isoxazolo[5,4-a]carbazole (**4e**): White amorphous powder (65%), m.p. 198–200°C. IR: ν_{max} 3376, 2923, 1642, 1575, 1440 cm^{-1}. NMR: δ_H 8.70 (br s, 1H, N10-H), 8.18–8.13 (d, 1H, C6-H, J = 7.84 Hz), 8.04–7.99 (d, 1H, C5-H, J = 8.24 Hz), 7.62–7.58 (d, 1H, C9-H, J = 8.08 Hz), 7.54–7.49 (m,1H, C8-H), 7.44–7.41 (d, 1H, C4-H, J = 8.24 Hz), 7.36–7.32 (m,1H, C7-H), 2.68 (s, 3H, C3-CH_3); δ_C 157.2, 145.1, 135.0, 134.6, 130.3, 127.4, 121.6, 120.4, 117.9, 110.6, 108.3, 106.0, 105.1 (13 aromatic C), 21.4 (C3-CH_3). MS: *m/z* (%) 222 (18). Anal. Calcd. for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60; Found: C, 75.76; H, 4.49; N, 12.64%.

Reaction of 2-acetyl-2,3,4,9-tetrahydro-1H-carbazol-1-ones (**3a-e**) *with hydrazine hydrate: General procedure*

To the appropriate 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**, 1 mmol) in glacial acetic acid (15 ml) was added hydrazine hydrate (2 mmol) and the whole was refluxed on an oil bath for 1 h. The reaction was monitored by TLC. After completion of the reaction the mixture was poured onto crushed ice. The precipitate was collected, washed with water, and dried. It was purified by column chromatography over silica gel using petroleum ether/ethyl acetate (successively 98 : 2 and 85 : 15) as eluant. The former fraction yielded the respective 1,10-dihydro-3-methylpyrazolo[3,4-*a*]carbazole (**5**), the latter the respective 3-methyl-1,4,5,10-tetrahydropyrazolo[3,4-*a*]carbazole (**6**).

1,10-Dihydro-3,9-dimethylpyrazolo[3,4-a]carbazole (**5a**): White powder (75%), m.p. 142–144°C. IR: ν_{max} 3275, 2934, 1630, 1574, 1458 cm^{-1}. NMR: δ_H 12.00 (br s, H, N1-H), 11.12 (br s, 1H, N10-H), 7.89–7.83 (d, 1H, C6-H, J = 8.84 Hz), 7.73–7.66 (d, 1H, C5-H, J = 8.48 Hz), 7.36–7.29 (d, 1H, C4-H, J = 8.48 Hz), 7.14–7.08 (d, 1H, C8-H, J = 7.00 Hz), 7.07–7.01 (m, 1H, C7-H), 2.55 (s, 3H, C9-CH_3), 2.49 (s, 3H, C3-CH_3); δ_C 142.1, 139.4, 132.3, 129.9, 128.7, 127.6, 122.3, 120.1, 118.9, 117.8, 116.3, 111.3, 107.5 (13 aromatic C), 20.7 (C9-CH_3), 18.6 (C3-CH_3). MS: *m/z* (%) 235 (42). Anal. Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86; Found: C, 76.60; H, 5.51; N, 17.82%.

3,9-Dimethyl-1,4,5,10-tetrahydropyrazolo[3,4-a]carbazole (**6a**): White powder (15%), m.p. 168–170°C. IR: ν_{max} 3253, 2923, 1624, 1576, 1446 cm^{-1}. NMR: δ_H 12.05 (br s, 1H, N1-H),11.13 (br s, 1H, N10-H), 7.90–7.82 (d, 1H, C6-H, J = 8.00 Hz), 7.19–7.01 (m, 2H, C7, C8-H), 3.00–2.89 (m, 2H, C5-H_2), 2.82–2.70 (m, 2H, C4-H_2), 2.57 (s, 3H, C9-CH_3), 2.23 (s, 3H, C3-CH_3); δ_C 142.8, 138.1, 130.7, 128.9, 124.1, 120.1, 119.0, 118.1, 114.3, 111.9, 108.4 (11 aromatic C), 28.7 (C9-CH_3), 24.4 (C5), 21.8 (C4), 20.7 (C3-CH_3). MS: *m/z* (%) 237 (40). Anal. Calcd. for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71; Found: C, 76.03; H, 6.32; N,17.76%.

1,10-Dihydro-3,8-dimethylpyrazolo[3,4-a]carbazole (**5b**): Pale yellow powder (80%), m.p. 164–166°C. IR: ν_{max} 3274, 2923, 1628, 1574, 1440 cm^{-1}. NMR: δ_H 12.43 (br s, 1H, N1-H), 11.17 (br s, 1H, N10-H), 8.01–7.96 (d, 1H, C5-H, J = 7.92 Hz), 7.77–7.72 (d, 1H, C6-H, J = 8.46 Hz), 7.45 (s, 1H, C9-H), 7.40–7.35 (d, 1H, C7-H, J = 8.46 Hz), 7.05–7.00 (d, 1H, C4-H, J = 7.92 Hz), 2.37 (s, 3H, C8-CH_3), 2.20 (s, 3H, C3-CH_3); δ_C 144.3, 138.5, 136.1, 130.9, 129.0, 128.1, 124.4, 122.1, 120.9, 114.3, 112.3, 108.4, 107.0 (13 aromatic C), 24.7 (C8-CH_3), 22.6 (C3-CH_3). MS: *m/z* (%) 235 (32). Anal. Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86; Found: C, 76.67; H, 5.63; N, 17.71%.

3,8-Dimethyl-1,4,5,10-tetrahydropyrazolo[3,4-a]carbazole (**6b**): Pale yellow powder (10%), m.p. 150–152°C. IR: ν_{max} 3250, 2919, 1630, 1576, 1440 cm^{-1}. NMR: δ_H 12.43 (br s, 1H, N1-H), 11.29 (br s, 1H, N10-H), 7.40 (s, 1H, C9-H), 7.04–6.95 (m, 2H, C6, C7-H), 2.61–2.51 (m, 4H, C4-H_2, C5-H_2), 2.40 (s, 3H, C8-CH_3), 2.20 (s, 3H, C3-CH_3); δ_C 146.4, 140.7, 135.1, 129.9, 122.8, 120.4, 118.0, 116.1, 113.3, 112.5, 106.9 (11 aromatic C), 28.0 (C8-CH_3), 25.7 (C5), 22.6 (C4), 19.7 (C3-CH_3). MS: *m/z* (%) 237 (28). Anal. Calcd. for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71; Found: C, 75.99; H, 6.31; N, 17.65%.

1,10-Dihydro-3,7-dimethylpyrazolo[3,4-a]carbazole (**5c**): Needles (65%), m.p. 157–159°C. IR: ν_{max} 3354, 2947, 1630, 1564, 1449 cm^{-1}. NMR: δ_H 12.47 (br s, 1H, N1-H), 11.04 (br s, 1H, N10-H), 7.91 (s, 1H, C6-H), 7.81–7.71 (d, 1H, C5-H, J = 8.24 Hz), 7.61–7.51 (d, 1H, C4-H, J = 8.24 Hz), 7.43–7.34 (d, 1H, C9-H, J = 8.00 Hz), 7.24–7.15 (d, 1H, C8-H, J = 8.00 Hz), 2.57 (s, 3H, C7-CH_3), 2.49 (s, 3H, C3-CH_3); δ_C 145.1, 138.6, 136.8, 131.5, 130.4, 127.6, 123.9, 120.4, 118.9, 116.9, 110.3, 108.4, 105.6 (thirteen aromatic C), 26.7 (C7-CH_3), 21.6 (C3-CH_3). MS: *m/z* (%) 235 (52). Anal. Calcd. for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86; Found: C, 76.59; H, 5.60; N, 17.9%.

3,7-Dimethyl-1,4,5,10-tetrahydropyrazolo[3,4-a]carbazole (**6c**): White powder (15%), m.p. 187–189°C. IR: ν_{max} 3253, 2923, 1628, 1574, 1445 cm^{-1}. NMR: δ_H 12.49 (br s, 1H, N1-H),11.07 (br s, 1H, N10-H), 7.92 (s, 1H, C6-H), 7.50–7.38 (d, 1 H, C9-H, J = 8.48 Hz), 7.50–7.38 (d, 1H, C8-H, J = 8.48 Hz), 2.79–2.61 (m, 2H, C5-H_2), 2.60–2.51 (m, 2H, C4-H_2), 2.45 (s, 3H, C7-CH_3), 2.05 (s, 3H, C3-CH_3); δ_C 148.1, 144.0, 135.1, 132.6, 123.1, 122.8, 118.6, 118.1, 112.5, 109.4, 105.7 (11 aromatic C), 26.7 (C7-CH_3), 22.4 (C5), 20.9 (C4), 19.4 (C3-CH_3). MS: *m/z* (%) 237 (28). Anal. Calcd. for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71; Found: C, 75.67; H, 6.29; N, 17.68%.

7-Chloro-1,10-dihydro-3-methylpyrazolo[3,4-a]carbazole (**5d**): White powder (70%), m.p. 167–169°C. IR: ν_{max} 3234, 2920, 1618, 1572, 1440 cm^{-1}. NMR: δ_H, 12.34 (br s, 1H, N1-H), 11.56 (br s, 1H, N10-H), 7.84–7.80 (d, 1H, C5-H, J = 8.54 Hz), 7.68–7.64 (d, 1H, C4-H, J = 8.54 Hz), 7.49–7.48 (d, 1H, C6-H, J_{meta} = 1.90 Hz), 7.32–7.28 (d, 1H, C9-H, J = 8.52 Hz), 7.03–6.98 (dd, 1H, C8-H, J_{ortho} = 8.52, J_{meta} = 1.90 Hz), 2.20 (s, 3H, C3-CH_3); δ_C 143.9, 140.4, 138.2, 137.1, 128.4, 126.6, 123.7, 120.1, 118.9, 114.4, 112.6, 110.1, 109.1 (13 aromatic C), 23.7 (C3-CH_3). MS: *m/z* (%) 255 (26). Anal. Calcd. for $C_{14}H_{10}ClN_3$: C, 65.76; H, 3.94; N, 16.43; Found: C, 65.89; H, 3.90; N, 16.40%.

7-Chloro-3-methyl-1,4,5,10-tetrahydropyrazolo[3,4-a]carbazole (**6d**): White powder (12%), m.p. 172–174°C. IR: ν_{max} KBr, 3218, 2923, 1627, 1579, 1440 cm^{-1}. NMR: δ_H 12.32 (br s, 1H, N1-H), 11.57 (br s, 1H, N10-H), 7.47 (s, 1H, C6-H), 7.32–7.25 (d, 1H, C9-H, J = 8.48 Hz), 7.03–6.96 (d, 1H, C8-H, J = 8.48 Hz), 2.90–2.83 (m, 2H, C5-H_2), 2.73–2.67 (m, 2H, C4-H_2), 2.19 (s, 3H, C3-CH_3); δ_C, 146.0, 141.9, 134.7, 130.9, 128.1, 120.6, 118.0, 115.1, 114.1, 112.9, 109.4 (11 aromatic C), 26.4 (C5), 22.3 (C4), 21.0 (C3-CH_3). MS: *m/z* (%) 237 (28). Anal. Calcd. for $C_{14}H_{12}ClN_3$: C, 65.25; H, 4.69; N, 16.30; Found: C, 65.05; H, 4.73; N, 16.39%.

1,10-Dihydro-3-methylpyrazolo[3,4-a]carbazole (**5e**): White powder (68%), m.p. 150–152°C. IR: ν_{max} 3216, 2923, 1627, 1580, 1444 cm^{-1}. NMR: δ_H 12.45 (br s, 1H, N1-H), 11.32 (br s, 1H, N10-H), 8.14–8.08 (d, 1H, C5-H, J = 7.92 Hz), 7.81–7.77(d, 1H, C9-H, J = 8.52 Hz), 7.67–7.62 (d, 1H C6-H, J = 7.96 Hz), 7.32–7.28 (d, 1H, C4-H, J = 7.92 Hz), 7.05–6.93 (m, 2H, C7, C8-H), 2.20 (s, 3H, C3-CH_3); δ_C 148.0, 144.2, 132.1, 131.9, 127.4, 127.3, 124.4, 124.1, 120.1, 118.9, 112.3, 110.4, 109.4 (13 aromatic C), 21.8 (C3-CH_3). MS: *m/z* (%) 221 (46). Anal. Calcd. for $C_{14}H_{11}N_3$: C, 76.00; H, 5.01; N, 18.99; Found: C, 75.89; H, 5.01; N, 19.03%.

3-Methyl-1,4,5,10-tetrahydropyrazolo[3,4-a]carbazole (**6e**): White powder (15%), m.p. 190–192°C. IR: ν_{max} 3218, 2923, 1627, 1579, 1440 cm^{-1}. NMR: δ_H 12.23 (br s, 1H, N1-H), 11.33 (br s, 1H, N10-H), 7.45–7.40 (d, 1H, C9-H, J = 7.60 Hz), 7.32–7.26 (d, 1H, C6-H, J = 7.88 Hz), 7.04–6.93 (m, 2H, C7, C8-H), 2.92–2.84 (m, 2H, C5-H_2), 2.73–2.67 (m, 2H, C4-H_2), 2.19 (s, 3H, C3-CH_3); δ_C 148.9, 144.3, 132.4, 129.9, 122.7, 120.1, 119.3, 118.0, 116.1, 111.9, 109.4 (11 aromatic C), 26.4 (C5), 24.3 (C4), 22.0 (C3-CH_3). MS: *m/z* (%) 223 (35). Anal. Calcd. for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82; Found: C, 75.51; H, 5.86; N, 18.88%.

Reaction of 2-acetyl-2,3,4,9-tetrahydro-1H-carbazol-1-ones (**3a-e**) *with semicarbazide hydrochloride: General procedure*

To the appropriate 2-acetyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**3**, 1 mmol) in glacial acetic acid (15 ml) was added semicarbazide hydrochloride (2 mmol) and the solution was refluxed on an oil bath for 1 h. The reaction was monitored by TLC. After the completion of the reaction it was poured onto crushed ice. The precipitate was filtered off, washed with water and dried. It was purified by column chromatography over silica gel using petroleum ether/ethyl acetate (98 : 2 to get the respective 1,10-dihydro-3-methylpyrazolo[3,4-*a*] carbazole (**5**).

1,10-Dihydro-3,9-dimethylpyrazolo[3,4-a]carbazole (**5a**): White powder (80%).

1,10-Dihydro-3,8-dimethylpyrazolo[3,4-a]carbazole (**5b**): Pale yellow powder (75%).

1,10-Dihydro-3,7-dimethylpyrazolo[3,4-a]carbazole (**5c**): Needles (78%).

7-Chloro-1,10-dihydro-3-methylpyrazolo[3,4-a]carbazole (**5d**): White powder (65%).

1,10-Dihydro-3-methylpyrazolo[3,4-a]carbazole (**5e**): White powder (75%).

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