Reactions of methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl) oxoacetates. Synthesis of methyl isoxazolo[5,4-*a*]carbazole-3-carboxylates

Arputharaj Ebenezer Martin and Karnam Jayarampillai Rajendra Prasad*

Department of Chemistry, Bharathiar University, Coimbatore- 641046, Tamil Nadu, India

The reaction of methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetates (**1a–e**) with hydroxylamine hydrochloride in alcoholic KOH afforded 1-hydroxyimino-2,3,4,9-tetrahydro-1*H*-carbazoles (**2a–e**), and in acetic acid methyl isoxazolo[5,4-*a*]carbazole-3-carboxylates (**3a–e**). Ketoesters **1a–e** with urea and thiourea under acidic conditions yielded a mixture of the respective 1-hydroxycarbazoles (**6a–e**) and 2,3,4,9-tetrahydro-1*H*-carbazol-1-ones (**7a–e**), but under basic conditions the respective 1-carbimido- and 1-thiocarbimido-2,3,4,9-tetrahydro-1*H*-carbazoles (**8a–e** and **9a–e**) were formed. Plausible mechanisms are proposed.

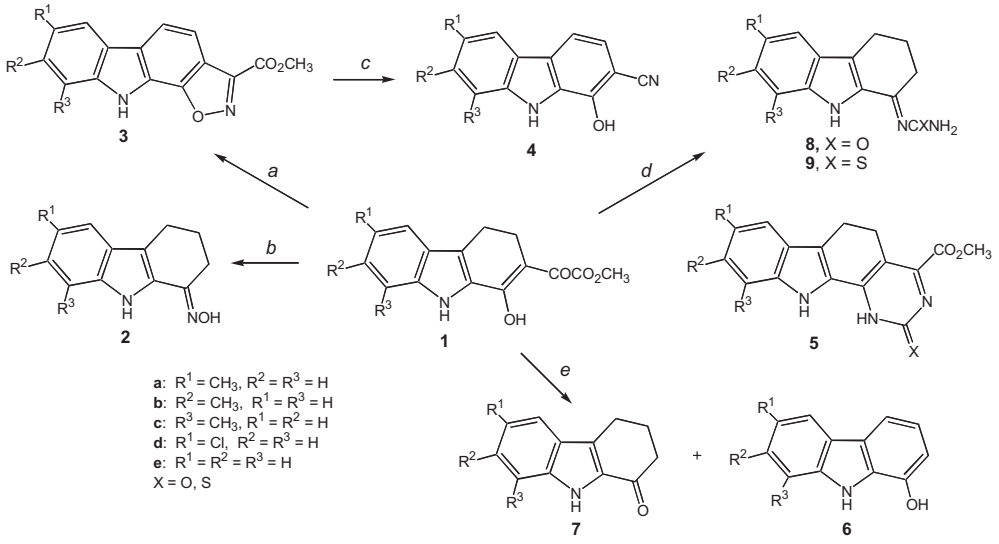
Keywords: carbazoles, fused isoxazoles, α-ketoesters

Carbazole-containing alkaloids have caught the attention of the chemists and biochemists because of their biological activities such as antitumor,[1-3] antibacterial,[4] antifungal[4] and anti-HIV.[5,6] Numerous total syntheses of natural compounds containing the carbazole system, as well as structural modifications in which various heterocyclic systems are annulated to the carbazoles, have been effected.[7,8] Interest in these modifications lies in the possible changes in biological activity. In this context, we focused our attention upon the synthesis of heteroannulated carbazoles from the easily accessible methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetates (**1a–e**).[9]

Results and discussion

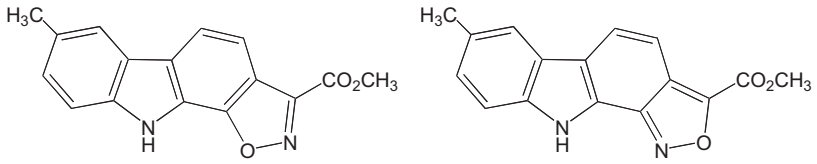
Our earlier work on methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetates (**1a–e**)[9] led us to investigate the reactions of **1** with hydroxylamine hydrochloride, urea and thiourea under basic and acidic conditions. With the aim of obtaining isoxazolo[5,4-*a*]carbazole-3-carboxylates from these easily accessible oxoacetates (**1**), we treated methyl 2-(6-methyl-1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetate (**1a**) with hydroxylamine hydrochloride in alcoholic KOH. The reaction was monitored by TLC. After completion of the reaction a brown solid was obtained which on column chromatography over silica gel yielded a dirty white spongy material melting at 144–146°C. It was characterised as 1-hydroxyimino-6-methyl-2,3,4,9-tetrahydro-1*H*-carbazole (**2a**) by mixed melting point (lit.[10] m.p. 138°C) and superimposable IR and NMR spectra. We consider that the base eliminated the glyoxalate residue from the ketoester **1a**, followed by oximation (Scheme 1).

Accordingly we carried out the same reaction under acidic conditions. Methyl 2-(6-methyl-1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetate (**1a**) with hydroxylamine hydrochloride in glacial acetic acid yielded after purification a pale yellow powder melting at 225–227°C. Its IR spectrum showed NH and ester carbonyl stretching bands at 3304 and 1735 cm^{-1}, respectively. The ^1H NMR spectrum in $CDCl_3$ showed one-proton broad singlet at δ 8.73 for carbazole NH, one-proton doublet between δ 8.12–8.06 (J = 8.4 Hz) for C4-H, one proton doublet at δ 7.97–7.96 (J = 1.0 Hz) for C6-H, one proton doublet centred at δ 7.94 (J = 8.4 Hz) for C5-H, one-proton doublet between δ 7.54–7.48 (J = 8.2 Hz) for C9-H, one proton doublet of doublets between δ 7.39 and 7.35 (J_{ortho} = 8.2 Hz; J_{meta} = 1.0 Hz) for C8-H, a three-proton singlet at δ 4.14 for the OCH_3 group and a three proton singlet at δ 2.58 was due to C7-CH_3. The ^{13}C NMR in $CDCl_3$ showed the presence of 14 carbons from δ 161.2 (ester C=O) to 111.2 (C5b), and at 52.9 (ester OCH_3) and 21.4 (C7-CH_3) (see Experimental). Here, and in the proton spectrum, a CH_2CH_2



Scheme 1 *Reagents: a:* $NH_2OH.HCl$, AcOH; *b*: $NH_2OH.HCl$, Alc. KOH; *c*: Alc. NaOH; *d*: H_2NCXNH_2, Alc. KOH; *e*: H_2NCXNH_2, AcOH.

* Correspondent. E-mail: prasad_125@yahoo.com



3a Steric energy: 23.1534 kcal/mol

3a' Steric energy: 23.6927 kcal/mol

Fig. 1

group was clearly not present. The molecular ion peak appeared at *m/z* 280 (96%). This, and the elemental analysis, agreed well with the molecular formula required for a fully aromatic isoxazolo-carbazole system. Although the spectral and analytical results were consistent with either of the two structures (**3a** and **3a'**) shown in Fig. 1, the structure **3a** is preferred over **3a'** based on the following points:

(i) The steric energies of the two structures were calculated using molecular mechanics calculation (MM2). This predicted that the structure **3a** whose steric energy is 23.1534 kcal/mol is 0.54 kcal/mol lower than that of structure **3a'**. The structure having [5,4-*a*] fusion of isoxazole to carbazole has lower energy than that having [3,4-*a*] fusion.

(ii) More conclusive evidence in favour of structure **3a** over **3a'** was obtained from chemical analysis. The hydrolysis and decarboxylation of **3a** under basic conditions produced 1-hydroxy-9*H*-carbazole-2-carbonitrile (**4a**). The formation of this product was confirmed on the basis of mixed m.p. and superimposable IR spectra with a sample prepared earlier in our group.[12] The IR spectrum of **4a** showed the presence of C≡N stretching at 2224 cm^{-1}. If the product from the reaction of **1** with hydroxylamine hydrochloride had been **3a'**, a nitrile would not have been formed.

From the above evidence the structure of the product was assigned as methyl 7-methylisoxazolo[5,4-*a*]carbazole-3-carboxylate (**3a**). The generality of these reactions was tested and confirmed with other methyl 2-(1-oxo-2,3,4,9-tetrahydro-*1H*-carbazol-2-yl)oxoacetates (**1b–e**).

We wished to obtain pyrimido[4,5-*a*]carbazoles (**5**) from the reaction of the potential precursors **1** with urea and thiourea. Therefore, we treated methyl 2-(6-methyl-1-oxo-2,3,4,9-tetrahydro-*1H*-carbazol-2-yl)oxoacetate (**1a**) with urea in glacial acetic acid. The reaction gave a mixture of two products which were separated by column chromatography over silica gel. The first product obtained from petroleum ether:ethyl acetate (98:2) fraction was found to be 6-methylcarbazol-1-ol (**6a**), which matched with all spectral and analytical data from the literature.[11] The second product, obtained on elution by petroleum ether:ethyl acetate (95:5), was simply the 6-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one[13] (**8a**) (mixed m.p., superimposable IR spectra). On mechanistic grounds, it can be supposed that the keto form of **1** loses the glyoxalate residue, followed by protonation, producing 1-oxo-1,2,3,4-tetrahydrocarbazole (**7**), while the enol form of **7** under the acidic conditions and on aerial oxidation may form the fully aromatised product, 1-hydroxycarbazole (**6**).

In a further attempt to obtain methyl 1,5,6,11-tetrahydro-2-oxo-2*H*-pyrimido[4,5-*a*]carbazole-4-carboxylates (**5**), we treated methyl 2-(6-methyl-1-oxo-2,3,4,9-tetrahydro-*1H*-carbazol-2-yl)oxoacetate (**1a**) with urea in alcoholic KOH. From this reaction we obtained a brown precipitate melting at 172–174°C. Its IR spectrum showed a band at 3273 cm^{-1} from N–H stretching. A sharp band at 1641 cm^{-1} was due to C=N stretching. Since the IR spectrum does not show a band around 1720 cm^{-1}, it was clear that the expected ester was not realised from this reaction, and this was further confirmed from its ^{1}H NMR spectrum. It showed a one proton broad singlet at δ 8.63 due to N9-H. A one proton singlet at δ 7.43 was due to C5-H. A two proton multiplet between δ 7.30 and 7.16 was due to the C7 and C8 protons. A 2H absorption between δ 6.18 and 6.06 was assigned to NH_2 protons. Three two-proton multiplets between δ 3.01–2.94, 2.67–2.62 and 2.29–2.22 were attributable to methylene protons at C4, C2 and C3, respectively, and a three-proton singlet at δ 2.45 was due to methyl protons at C6. The absence of resonance from a CO_2CH_3 group was further evidence contra-indicating **5a**. The structure 1-carbimido-6-methyl-2,3,4,9-tetrahydro-1*H*-carbazole (**8a**) was attested by the appearance of the molecular ion peak at *m/z* 241 (12%) in its mass spectrum, and by microanalytical data.

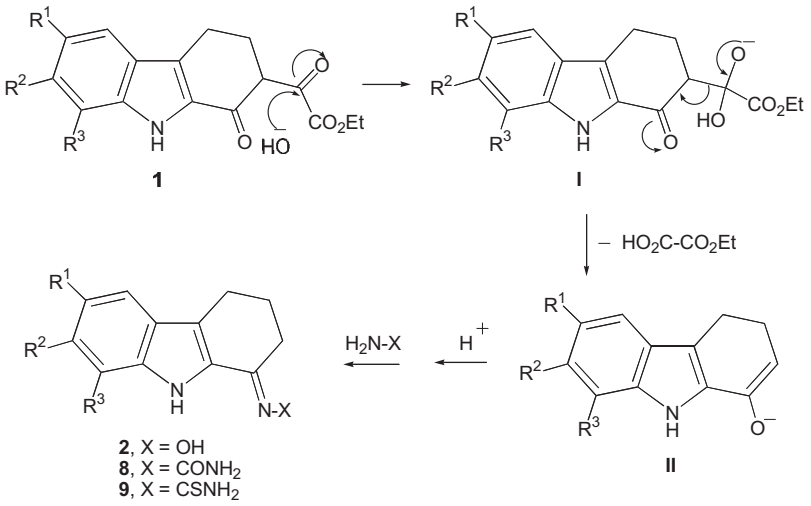
Similarly, the reaction with thiourea yielded a brown solid melted at 146–148°C. The IR spectrum showed a band at 3273 cm^{-1} for N-H stretching. A strong band at 1641 cm^{-1} was due to C=N stretching, and a medium-intensity peak at 1184 cm^{-1} was attributable to C=S stretching. Its ^{1}H NMR spectrum showed a one proton broad singlet at δ 11.44 was due to N9-H and a two proton multiplet centred at δ 6.50 due to NH_2 protons. The rest of the proton spectrum was in its CH absorptions very similar to that of compound **8a**. In its mass spectrum the molecular ion peak appeared at *m/z* 257 (10%). The elemental analysis and the spectral details were in agreement with the structure as 1-thiocarbimido-6-methyl-2,3,4,9-tetrahydro-1*H*-carbazole (**9a**) for the product. Under acidic conditions, the reaction of **1a** with thiourea produced 1-hydroxy-6-methylcarbazole (**6a**) and 6-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**7a**), as was observed also in the case of urea. These reactions were found to be general for all carbazole derivatives **1** (Scheme 1).

A plausible mechanism for the formation of **8** rather than **5** can be proposed (Scheme 2). First the intermolecular nucleophilic hydroxide ion attack favoured over the intermolecular nucleophilic NH_2 attack at α-carbonyl carbon of methyl glyoxalate moiety to give the intermediate **I**. Then the elimination of monomethyl oxalate followed by the condensation of the urea NH_2 group with the C1 carbonyl group took place to yield the intermediate **II**. Finally, neutralisation with dilute HCl afforded the isolated product **8**. Similar types of mechanism were possible for the formation of **2** as well as of **9**.

We conclude that under basic conditions compound **1** reacts with hydroxylamine, urea and thiourea in a similar manner, Under acidic conditions the reaction of hydroxylamine hydrochloride yielded the desired product, but the reactions of urea and thiourea were not so fruitful.

Experimental

Melting points were determined by using Mettler FP 51 apparatus (Mettler Instruments, Switzerland). IR spectra were recorded using the KBr disc technique on a Shimadzu FTIR-8201PC spectrophotometer (Shimadzu, Japan). ^{1}H NMR spectra were recorded in $CDCl_3$ and/or DMSO-d_6 on a Varian AMX 400 FT-NMR (Varian Australia) using TMS as internal standard. Mass spectra were recorded on Jeol-JMS-D-300 mass spectrometer (Jeol, Japan), using 70 eV ionisation in



Scheme 2 Mechanism for the formation of **2**, **8** and **9**

EI mode. Microanalyses were carried out 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 and ethyl acetate (85:15) as the developing solvents.

Methyl isoxazolo[5,4-a]carbazole-3-carboxylates (**3a–e**): *general procedure*

To the appropriate methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetate (**1**, 1 mmol) in glacial acetic acid (15 ml) was added hydroxylamine hydrochloride (0.14 g, 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 into crushed ice. The precipitate was filtered, washed with water and dried. It was purified by column chromatography over silica gel using petroleum ether:ethyl acetate (85:15) as eluant.

Methyl 7-methylisoxazolo[5,4-a]carbazole-3-carboxylate (**3a**): Pale yellow powder (0.18 g, 65%), m.p. 225–227°C. IR: ν_{max} 3304, 2960, 1735, 1645, 1445, 1260, 1001 cm^{-1}. NMR ($CDCl_3$): δ_H 8.73 (b s, 1H, N10-H), 8.12–8.06 (d, 1H, C4-H, J = 8.4 Hz), 7.97–7.96 (d, 1H, C6-H, J_{meta} = 1.0 Hz), 7.98–7.90 (d, 1H, C5–H, J = 8.4 Hz), 7.54–7.48 (d, 1H, C9-H, J = 8.2 Hz), 7.39–7.35 (d d, 1H, C8-H, J_{ortho} = 8.2 Hz, J_{meta} = 1.0 Hz), 4.14 (s, 3H, OCH_3), 2.58 (s, 3H, C7-CH_3); δ_C 161.2 (ester C=O), 158.5 (C10b), 142.1 (C3), 130.2 (C5a), 128.4 (C7), 128.0 (C9a), 125.7 (C4), 123.2 (C3a), 120.5 (C5), 118.2 (C8), 112.7 (C6), 112.4 (C9), 112.2 (C10a), 111.2 (C5b), 52.9 (OCH_3), 21.4 (C7-CH_3). MS: *m/z* (%) 280 (96, M$^+$), 279 (12), 221 (40), 195 (10), 193 (15), 155 (100). Anal. Calcd. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99; Found: C, 68.46; H, 4.38; N, 9.88%.

Methyl 8-methylisoxazolo[5,4-a]carbazole-3-carboxylate (**3b**): Pale yellow powder (0.20 g, 70%), m.p. 235–238°C. IR: ν_{max} 3350, 2962, 1732, 1650, 1446, 1261, 1023 cm^{-1}. NMR ($CDCl_3$): δ_H 8.73 (br. s, 1H, N10-H), 8.10–8.05 (d, 1H, C4-H, J = 8.4 Hz), 8.04–8.01 (d, 1H, C6-H, J = 7.9 Hz), 7.91–7.87 (d, 1H, C5 –H, J = 8.42 Hz), 7.40 (s, 1H, C9-H), 7.20–7.17 (d, 1H, C8-H, J = 7.9 Hz), 4.13 (s, 3H, OCH_3), 2.58 (s, 3H, C8-CH_3); δ_C 164.2 (ester C=O), 160.0 (C10b), 141.3 (C3), 129.6 (C5a), 126.4 (C8), 121.3 (C9a), 122.8 (C4), 123.2 (C3a), 121.1 (C5), 118.2 (C8), 121.7 (C6), 122.4 (C9), 109.2 (C10a), 130.4 (C5b), 53.4 (OCH_3), 20.8 (C8-CH_3). MS: *m/z* (%) 280 (100, M$^+$), 279 (50), 193 (88), 192 (45), 155 (98), 115 (24). Anal. Calcd. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99; Found: C, 68.50; H, 4.33; N, 10.08%.

Methyl 9-methylisoxazolo[5,4-a]carbazole-3-carboxylate (**3c**): Dingy coloured solid (0.185 g, 66%), m.p. 220–223°C. IR: ν_{max} 3251, 2950, 1734, 1630, 1445, 1122 cm^{-1}. NMR ($CDCl_3$): δ_H 8.76 (b s, 1H, N10-H), 8.14–8.09 (d, 1H, C8-H, J = 7.4 Hz), 8.03–7.99 (d, 1H, C5-H, J = 7.6 Hz), 7.95–7.88 (m, 1H, C7 –H), 7.37–7.32 (d, 1H, C4-H, J = 7.6 Hz), 7.31–7.27 (d, 1H, C6-H, J = 7.6 Hz), 4.14 (s, 3H, OCH_3), 2.67 (s, 3H, C9-CH_3); δ_C 166.4 (ester C=O), 161.3 (C10b), 147.0 (C3), 131.7 (C5a), 129.6 (C9a), 123.1 (C3a), 122.3 (C4), 120.8 (C5), 120.4 (C7), 120.1 (C9), 118.9 (C8), 118.4 (C6), 115.8 (C10a), 111.2 (C5b), 52.0 (OCH_3), 20.7 (C9-CH_3). MS: *m/z* (%) 280 (100, M$^+$), 249 (44), 194 (24), 193 (96), 192 (33), 155 (98), 143 (22), 115 (20). Anal. Calcd. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99; Found: C, 68.66; H, 4.33; N, 9.93%.

Methyl 7-chloroisoxazolo[5,4-a]carbazole-3-carboxylate (**3d**): Yellow powder (0.19 g, 64%), m.p. 240–243°C. IR: ν_{max} 3354, 2952, 1730, 1643, 1444, 1120, 999 cm^{-1}. NMR ($CDCl_3$): δ_H 8.76 (br s, 1H, N10-H), 7.89–7.83 (d, 1H, C5-H, J = 8.5 Hz), 7.82–7.78 (d, 1H, C4-H, J = 8.5 Hz), 7.74–7.72 (d, 1H, C6–H, J_{meta} = 1.8 Hz), 7.68–7.63 (d, 1H, C9-H, J = 8.7 Hz), 7.54–7.50 (d d, 1H, C8-H J_{ortho} = 8.7 Hz, J_{meta} = 1.8 Hz), 4.05 (s, 3H, OCH_3); δ_C 167.7 (ester C=O), 161.7 (C10b), 145.7 (C6), 142.1 (C3), 129.2 (C5a), 128.4 (C7), 128.0 (C9a), 125.7 (C4), 123.2 (C3a), 120.5 (C5), 118.2 (C8), 112.4 (C9), 112.2 (C10a), 111.2 (C5b), 52.9 (OCH_3). MS: *m/z* (%) 300 (100 M$^+$), 299 (32), 269 (56), 213 (80), 193 (26). Anal. Calcd. for $C_{15}H_9ClN_2O_3$: C, 59.91; H, 3.02; N, 9.32; Found: C, 59.86; H, 3.03; N, 9.37%.

Methyl isoxazolo[5,4-a]carbazole-3-carboxylate (**3e**): Dingy coloured solid (0.16 g, 60%), m.p. 238–240°C. IR: ν_{max} 3304, 2923, 1732, 1655, 1441, 1260, 1000 cm^{-1}. NMR ($CDCl_3$): δ_H 8.85 (b s, 1H, N10-H), 8.20–8.15 (d, 1H, C9-H, J = 7.8 Hz), 8.14–8.10 (d, 1H, C5-H, J = 8.4 Hz), 7.94–7.90 (d, 1H, C4–H, J = 8.4 Hz), 7.64–7.59 (d, 1H, C6-H, J = 8.2 Hz), 7.57–7.50 (m, 1H, C7-H), 7.39–7.32 (m, 1H, C8-H), 4.14 (s, 3H, OCH_3); δ_C 158.7 (ester C=O), 142.6, 134.9, 133.2, 128.6, 126.3, 123.1, 123.4, 122.4, 120.1, 119.9, 117.4, 112.2, 110.9, 52.4; MS: *m/z* (%) 266 (100, M$^+$), 255 (50), 199 (92), 159 (24), 121 (32). Anal. Calcd. for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52; Found: C, 67.76; H, 3.77; N, 10.55%.

Hydrolysis and decarboxylation of methyl isoxazolo[5,4-a]carbazole-3-carboxylates (**3a–e**), *general procedure*

To the appropriate methyl isoxazolo[5,4-*a*]carbazole-3-carboxylate (**3**, 0.5 mmol) in ethanol (15 ml) was added 10% aqueous sodium hydroxide (5 ml) and the whole was refluxed on an oil bath for 1 h. The reaction was monitored by TLC. After the completion of the reaction it was poured into crushed ice. It was extracted using ethyl acetate and the aqueous layer was collected and neutralised with cold aqueous HCl. The solid which separated was filtered, washed with water and dried.

1-Hydroxy-6-methyl-9H-carbazole-2-carbonitrile (**4a**): White powder (76 mg, 75%), m.p. 216–218°C (Lit.[12] 220°C).

1-Hydroxy-7-methyl-9H-carbazole-2-carbonitrile (**4b**): Brown powder (61 mg, 60%), m.p. 220–222°C (Lit.[12] 215°C).

1-Hydroxy-8-methyl-9H-carbazole-2-carbonitrile (**4c**): Dirty white powder (69 mg, 68%), m.p. 234–236°C (Lit.[12] 230°C).

6-Chloro-1-hydroxy-9H-carbazole-2-carbonitrile (**4d**): White powder (58 mg, 52%), m.p. 246–248°C (Lit.[12] 240°C).

Reaction of methyl 2-(1-oxo-2,3,4,9-tetrahydro-1H-carbazol-2-yl) oxoacetates (**1a–e**) *with urea*

The respective methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl) oxoacetate (**1**, 1 mmol) in alcoholic KOH (5 g in 20 ml EtOH) was refluxed with urea (1 mmol) for 8 h. The reaction was monitored by TLC. After completion of the reaction the solvent was evaporated, cooled, poured into crushed ice, washed with water, filtered, dried and recrystallised from ethanol.

1-Carbimido-6-methyl-2,3,4,9-tetrahydro-1H-carbazole (**8a**): Brown powder (0.16 g, 65%), m.p. 172–174°C. IR: ν_{max} 3273, 2924, 2858, 1641, 1541, 1481, 1325 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.63 (br s, 1H, N9-H), 7.43 (s,1H, C5-H), 7.30–7.16 (m, 2H, C7-, C8-H), 6.18–6.06 (m, 2H, $CONH_2$), 3.01–2.94 (m, 2H, C4-H_2), 2.67–2.62 (m,

2H, C2-H_2), 2.45 (s, 3H, C6-CH_3), 2.29–2.22 (m, 2H, C3-H_2). MS: *m/z* (%) 241 (12, M^+), 225 (10), 199 (100), 198 (30), 168 (11), 157 (22), 143 (95), 115 (30). Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.26; N, 17.41. Found: C, 69.45; H, 6.14; N, 17.09%.

1-Carbimido-7-methyl-2,3,4,9-tetrahydro-1H-carbazole (**8b**): Brown powder (0.154 g, 64%), m.p. 178–180°C. IR: ν_{max} 3269, 2926, 2858, 1636, 1539, 1470, 1323 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.66 (b s, 1H, N9-H), 7.56–7.49 (d, 1H, C5-H, *J* = 8.3 Hz), 7.16 (s,1H, C8-H), 7.00–6.94 (d, 1H, C6-H, *J* = 8.3 Hz), 6.15–6.03 (m, 2H, $CONH_2$), 3.02–2.94 (m, 2H, C4-H_2), 2.66–2.59 (m, 2H, C2-H_2), 2.47 (s, 3H, C7-CH_3), 2.30–2.21 (m, 2H, C3-H_2). MS: *m/z* (%) 241 (15, M^+), 226 (16), 225 (11), 199 (100), 198 (25), 157 (32), 143 (90), 115 (38). Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.26; N, 17.41. Found: C, 69.33; H, 6.12; N, 17.22%.

1-Carbimido-8-methyl-2,3,4,9-tetrahydro-1H-carbazole (**8c**): Brown powder (0.15 g, 63%), m.p. 194–196°C. IR: ν_{max} 3292, 2924, 2856, 1616, 1549, 1475, 1327 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.82 (b s, 1H, N9-H), 7.68–7.65 (d, 1H, C5-H, *J* = 8.0 Hz), 7.31–7.00 (m, 2H, C6, C7-H), 6.34–6.27 (m, 2H, $CONH_2$), 3.05–2.97 (m, 2H, C4-H_2), 2.70–2.64 (m, 2H, C2-H_2), 2.49 (s, 3H, C8-CH_3), 2.31–2.22 (m, 2H, C3-H_2). MS: *m/z* (%) 241(10, M^+), 225 (16), 199 (100), 198 (20), 168 (16), 157 (36), 131 (10), 115 (32). Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.26; N, 17.41. Found: C, 69.42; H, 6.20; N, 17.16%.

1-Carbimido-6-chloro-2,3,4,9-tetrahydro-1H-carbazole (**8d**): Brown powder (0.17 g, 64%), m.p. 210–212°C. IR: ν_{max} 3273, 2924, 2858, 1641, 1541, 1481, 1325 cm^{-1}. ^1H NMR ($CDCl_3$): δ 9.29 (b s, 1H, N_9-H), 7.62 (s,1H, C_5-H), 7.43–7.29 (m, 2H, C_7- C_8-H), 6.26–6.12 (m, 2H, C_1-$NCONH_2$), 3.04–2.93 (m, 2H, C_4-H_2), 2.73–2.63 (m, 2H, C_2-H_2), 2.34–2.22 (m, 2H, C_3-H_2); MS: *m/z* (%) 261(20, M^+), 246 (10), 245 (16), 219 (100), 188 (14), 177 (24), 151 (16), 149 (10). Anal. Calcd. for $C_{13}H_{12}ClN_3O$: C, 59.66; H, 4.62; N, 16.06. Found: C, 59.72; H, 4.54; N, 15.86%.

1-Carbimido-2,3,4,9-tetrahydro-1H-carbazole (**8e**): Brown powder (0.14 g, 62%), m.p. 187–189°C. IR: ν_{max} 3269, 2930, 2858, 1645, 1575, 1539, 1473, 1331 cm^{-1}. ^1H NMR ($CDCl_3$): δ 9.08 (b s, 1H, N9-H), 7.69–7.62 (d, 1H, C5-H, *J* = 8.0 Hz), 7.46–7.41 (d, 1H, C8-H, *J* = 8.2 Hz), 7.40–7.33 (m, 1H, C6-H), 7.19–7.11 (m, 1H, C7-H), 6.21–6.11 (m, 2H, $CONH_2$), 3.05–2.97 (m, 2H, C4-H_2), 2.71–2.62 (m, 2H, C2-H_2), 2.32–2.22 (m, 2H, C3-H_2). MS: *m/z* (%) 227 (16, M^+), 211 (16), 185 (100), 183 (16), 143 (16), 117 (20), 115 (32). Anal. Calcd. for $C_{13}H_{13}N_3O$: C, 68.70; H, 5.77; N, 18.49. Found: C, 68.33; H, 5.65; N, 18.16%.

Reaction of methyl 2-(1-oxo-2,3,4,9-tetrahydro-1H-carbazol-2-yl) oxoacetates (**1a–e**) *with thiourea*

The respective methyl 2-(1-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-2-yl)oxoacetate (**1**, 1 mmol) in alcoholic KOH (5 g in 20 ml EtOH) was refluxed with thiourea (1 mmol) for 8 h. The reaction was monitored by TLC. After completion of the reaction the solvent was evaporated, cooled, poured into crushed ice, washed with water, filtered, dried and recrystallised from ethanol.

1-Thiocarbimido-6-methyl-2,3,4,9-tetrahydro-1H-carbazole (**9a**): Brown powder (0.16 g, 62%), m.p. 146–148°C. IR: ν_{max} 3273, 2922, 2862, 1641, 1537, 1481, 1440, 1321 cm^{-1}. ^1H NMR ($CDCl_3$): δ 11.44 (br s, 1H, N9-H), 7.44 (s,1H, C5-H), 7.32–7.27 (d, 1H, C8-H, *J* = 8.4 Hz), 7.18–7.12 (d, 1H, C7-H, *J* = 8.4 Hz), 6.54–6.46 (m, 2H, $CSNH_2$), 2.95–2.90 (m, 2H, C4-H_2), 2.59–2.52 (m, 2H, C2-H_2), 2.39 (s, 3H, C6-CH_3), 2.19–2.11 (m, 2H, C3-H_2). MS: *m/z* (%) 257 (10, M^+), 256 (15), 200 (20), 199 (100), 185 (13), 170 (32), 157 (20), 143 (85). Anal. Calcd. for $C_{14}H_{15}N_3S$: C, 65.34; H, 5.87; N, 16.33. Found: C, 65.11; H, 5.73; N, 15.98%.

1-Thiocarbimido-7-methyl-2,3,4,9-tetrahydro-1H-carbazole (**9b**): Brown powder (0.162 g, 63%), m.p. 135–137°C. IR: ν_{max} 3261, 2932, 2860, 1636, 1537, 1470, 1327 cm^{-1}. ^1H NMR ($CDCl_3$): δ 11.42 (b s, 1H, N9-H), 7.57–7.53 (d, 1H, C5-H, *J* = 8.2 Hz), 7.19 (s,1H, C8-H), 6.94–6.90 (d, 1H, C6-H, *J* = 8.2 Hz), 6.80–6.74 (m, 2H, $CSNH_2$), 2.95–2.90 (m, 2H, C4-H_2), 2.62 (s, 3H, C7-CH_3), 2.55–2.50 (m, 2H, C2-H_2), 2.19–2.11 (m, 2H, C3-H_2). MS: *m/z* (%) 257 (8, M^+), 256 (20), 200 (15), 199 (100), 185 (20), 171 (16), 170 (40), 143 (78). Anal. Calcd. for $C_{14}H_{15}N_3S$: C, 65.34; H, 5.87; N, 16.33. Found: C, 65.71; H, 5.77; N, 15.91%.

1-Thiocarbimido-8-methyl-2,3,4,9-tetrahydro-1H-carbazole (**9c**): Brown powder (0.175 g, 68%), m.p. 142–144°C. IR: ν_{max} 3234, 2924, 2854, 1641, 1618, 1545, 1327 cm^{-1}. ^1H NMR ($CDCl_3$): δ 11.57 (br s, 1H, N9-H), 7.50–7.48 (d, 1H, C5-H, *J* = 7.8 Hz), 7.21–6.98 (m, 2H, C6, C7-H), 6.81–6.69 (m, 2H, $CSNH_2$), 3.05–2.96 (m, 2H, C4-H_2), 2.61–2.54 (m, 2H, C2-H_2), 2.51 (s, 3H, C8-CH_3), 2.20–2.12 (m, 2H, C3-H_2). MS: *m/z* (%) 257 (4, M^+), 256 (16), 200 (20), 199 (100), 198 (35), 170 (36), 157 (28), 143 (92). Anal. Calcd. for $C_{14}H_{15}N_3S$: C, 65.34; H, 5.87; N, 16.33. Found: C, 65.09; H, 5.67; N, 15.95%.

6-Chloro-1-thiocarbimido-2,3,4,9-tetrahydro-1H-carbazole (**9d**): Brown powder, (0.19 g, 69%), m.p. 151–153°C. IR: ν_{max} 3269, 2933, 2858, 1641, 1535, 1468, 1319 cm^{-1}. ^1H NMR ($CDCl_3$): δ 11.79 (b s, 1H, N9-H), 7.76 (s, 1H, C5-H), 7.40–7.37 (d, 1H, C8-H, *J* = 8.2 Hz), 7.32–7.29 (d, 1H, C7-H, *J* = 8.2 Hz), 6.59–6.50 (m, 2H, $CSNH_2$), 3.05–2.88 (m, 2H, C4-H_2), 2.64–2.50 (m, 2H, C2-H_2), 2.22–2.09 (m, 2H, C3-H_2). MS: *m/z* (%) 277 (10, M^+), 220 (16), 220 (20), 219 (100), 191 (22), 190 (18), 177 (16), 163 (75). Anal. Calcd. for $C_{13}H_{12}ClN_3S$: C, 56.21; H, 4.35; N, 15.13. Found: C, 56.00; H, 4.23; N, 15.98%.

1-Thiocarbimido-2,3,4,9-tetrahydro-1H-carbazole (**9e**): Brown powder (0.15 g, 62%), m.p. 137–139°C. IR: ν_{max} 3275, 2930, 2860, 1645, 1539, 1472, 1331 cm^{-1}. ^1H NMR ($CDCl_3$): δ 11.57 (b s, 1H, N9-H), 7.70–7.62 (d, 1H, C5-H, *J* = 7.8 Hz), 7.42–7.39 (d, 1H, C8-H, *J* = 8.3 Hz), 7.34–7.28 (m, 1H, C7-H), 7.13–7.05 (m, 1H, C6-H), 6.58–6.44 (m, 2H, $CSNH_2$), 3.02–2.93 (m, 2H, C4-H_2), 2.62-2.55 (m, 2H, C2-H_2), 2.23-2.13 (m, 2H, C3-H_2). MS: *m/z* (%) 243 (14, M^+), 242 (16), 185 (100), 183 (22), 171 (18), 156 (24), 143 (32), 129 (83). Anal. Calcd. for $C_{13}H_{13}N_3S$: C, 64.17; H, 5.38; N, 17.27. Found: C, 64.54; H, 5.22; N, 17.06%.

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