Synthesis of pyrazolino- and thiopyrimido- fused carbazoles from 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones

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Annelated carbazoles namely, 3-methyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-*a*]carbazoles, **4a–e** and 4-methyl-1,3,4,5,6,11-hexahydropyrimido[4,5-*a*]carbazole-2-thiones **5a–e** were synthesised in excellent yields from 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones **2a–e**, derived from the easily accessible 3,4-dihydrocarbazol-1(2*H*)-ones **1a–e**.

Keywords: 3,4-dihydrocarbazol-1(2*H*)-ones, dimethylcarbonate, 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones, pyrazolinocarbazoles and thiopyrimidocarbazoles

Over the past decades a large number of carbazole alkaloids have been obtained from terrestrial plants, marine resources and streptomycetes.[1-5] Their isolation has induced novel strategies towards the synthesis of newer carbazole derivatives. Development of new methods for the synthesis of functionalised carbazoles is attracting organic chemists due to the discovery of many carbazole alkaloids with varied biological activities.[6-9] Often heterocyclic annealated carbazoles have gained much importance due to their wide range of pharmacological properties. The biological activity of such annelated carbazoles is mostly based on their special affinity to DNA. Therefore these compounds have a major role for the discovery of antitumour active drugs.[9,12] The 2- and 3- carboxy derivatives of carbazoles[10] have been extensively used for the synthesis of anticancer alkaloids such as ellipticine and olivacine as well as of other pyrido[4,3-*b*]carbazole derivatives.[11-16]

Considering the importance of the annelated carbazole derivatives, we aimed to devise a simple method to synthesise methyl-1-oxo-1,2,3,4-tetrahydrocarbazole-carboxylates **3** from 3,4-dihydrocarbazol-1(2*H*)-ones[17] **1**. The intermediate thus isolated could be an important synthon towards the preparation of many annelated carbazoles and dimethylcarbonate was chosen as a reactant, because it is a well known methylating and methoxycarbonylating agent.[18] To date, no general methodology exists for the synthesis of functionalised 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones **2**. We now report with the synthesis and characterisation of hitherto unknown, 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones **2** and its utility in the preparation of pyrazolino- and thiopyrimido-fused carbazoles.

In this connection, we treated 3,4-dihydrocarbazol-1(2*H*)-ones **1** with dimethylcarbonate in sodium hydride in presence of ethanol, as a initiator of the reaction. We expected the formation of methyl-1-oxo-1,2,3,4-tetrahydrocarbazole-2-carboxylates **3**, but surprisingly we ended up with a new product namely 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones **2**. The reason for the formation of the product was that, the ethanol added to initiate the reaction had taken part in the reaction as a reactant instead of the dimethylcarbonate. 8-Methyl-3,4-dihydrocarbazol-1(2*H*)-one **1a** was reacted with dimethylcarbonate in sodium hydride in presence of absolute ethanol which yielded a yellow crystalline product with melting point, 162 °C. The product **2a** in its IR spectra showed a strong absorption at 3283 cm^{-1} corresponding to the NH vibrations. A sharp band at 1659 cm^{-1} showed the presence of the free carbonyl group The ^1H NMR spectrum showed a singlet with a three-proton intensity at δ 2.50 corresponding to the C_8–CH_3 protons. The presence of the ethylidene-methyl protons was inferred as a doublet at δ 1.93 with a *J* value of 7.20 Hz. The four-methylene protons at the C_3 and C_4 positions resonated as a multiplet in the region δ 2.99–3.09. A quartet at δ 6.96 appeared was due to the vinylidene proton of the C_2 carbon with *J* = 7.20 Hz. The aromatic proton at C_6 resonated as a multiplet in the region δ 7.05–7.10. The C_5 proton appeared as a doublet at δ 7.17 with the *J* value of 7.00 Hz. Another doublet resonated at δ 7.51 with a coupling constant value of 7.86 Hz, was due to the C_7 proton. The carbazole–NH proton appeared as a broad singlet at δ 8.91. Further the appearance of the molecular ion peak at *m*/*z* 225 (52%) in its mass spectrum and the elemental analysis, C: 80.09, N: 6.59, H: 6.28 % also agreed well with the molecular formula, $C_{15}H_{15}NO$. From the spectral and analytical data, the structure of the above compound was found to be 8-methyl-2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-one **2a** instead of methyl-8-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole-2-carboxylate **3a** as expected. A similar series of compounds were obtained by repeating the experiment on **1b–e** to realise the respective 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-ones as **2b**, **2c**, **2d** and **2e** (Scheme 1).

In order to test the role of dimethylcarbonate the following reactions were performed: (i) 3,4-dihydrocarbazol-1(2*H*)-one **1** was reacted with acetaldehyde in the presence of NaH, the reaction did not proceed; (ii) the reaction of **1** with acetaldehyde in NaH in the presence of dimethylcarbonate also failed; (iii) in order to make the preparation of **2** easier, **1** was reacted with acetaldehyde under mixed aldol condensation reaction conditions but the reaction didn't proceed; and (iv) the reaction of the other aldehydes with **1** had resulted in the formation of their respective arylidene-3,4-dihydrocarbazol-1(2*H*)-ones.[19–21]

Note that in the absence of dimethylcarbonate and only in the presence of ethanol we got the same product, but in low yields about 10–12%. It was concluded from our findings that the dimethylcarbonate added as reactant, has only catalysed the reaction in the formation of **2** which was further supported by the negative results obtained when methanol was added instead of ethanol.

Based on the above reaction conditions, the plausible mechanism for the formation of **2** might be as follows. The compound **1** is methoxycarbonylated *in situ* at the α-position (C_2) as expected, and subsequently the highly acidic proton flanked between the two carbonyl groups at C_2–H is eliminated under basic conditions to generate the carbanion intermediate **6**, which subsequently attacks the electrophile $CH_3CH_2^+$ generated from ethanol to give the intermediate **7**. Then the hydroxide ion attacks the more electrophilic centre of the carbonyl carbon of the ester to form the intermediate **8**. This eliminates (subsequently as carbon dioxide and methanol under basic conditions) to generate a new carbanion intermediate **9**, which loses the hydride ion (possibly as hydrogen molecule from H^- and H^+) gives the

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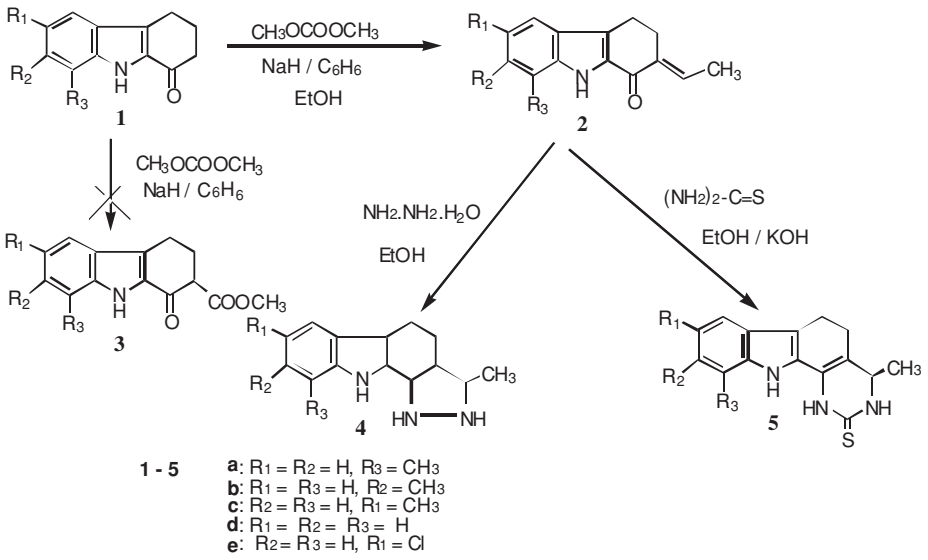
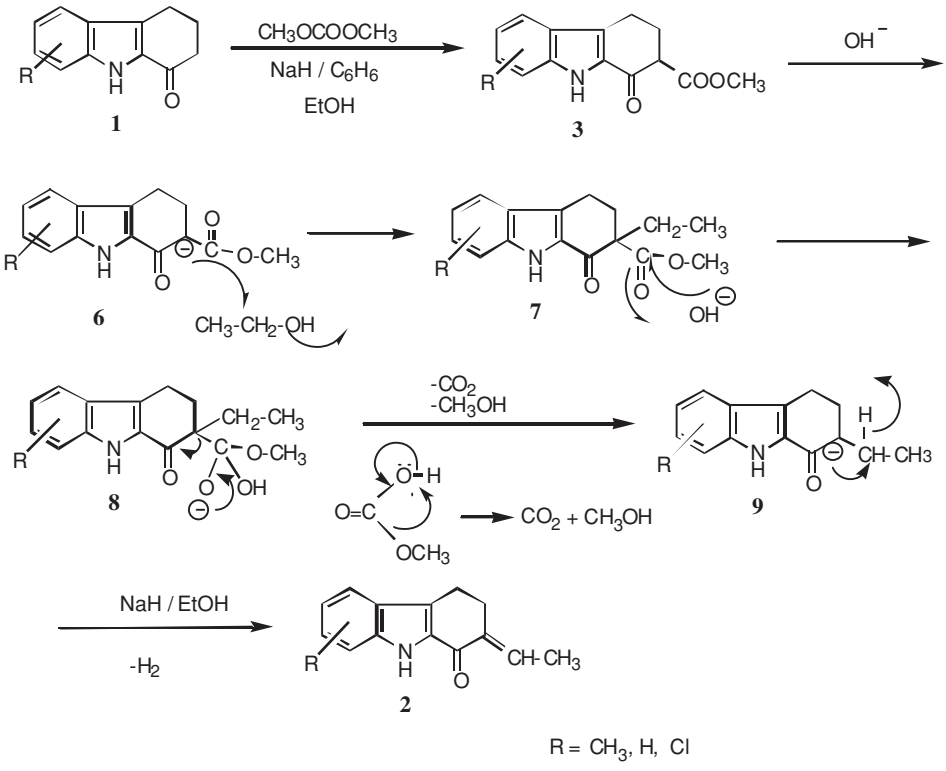


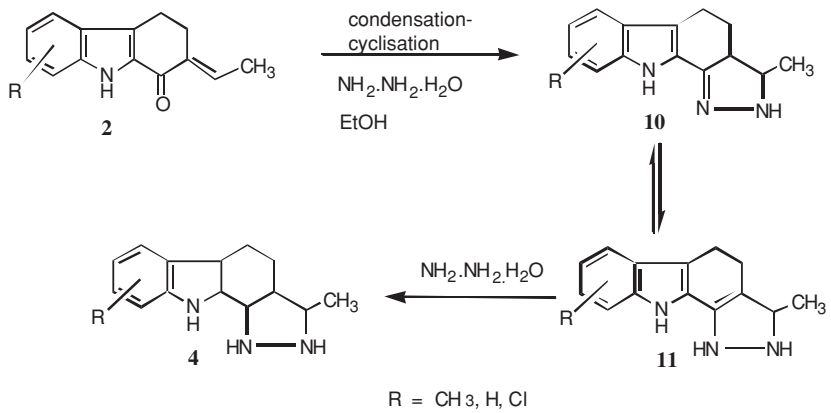
Scheme 1

more stable, crossed conjugated exocyclic α,β-unsaturated carbonyl group substituted carbazole system (Scheme 2).

The above synthon, 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-one **2** was utilised in the synthesis of fused annelated carbazoles. The reaction of **2a** with hydrazine hydrate in ethanol afforded a single product inferred from TLC. The IR spectrum of the compound showed the absence of the free carbonyl group and a strong band at 1328 cm^{-1} indicated the presence of C-N group. Further three strong bands at 3490, 3410 and 3277 cm^{-1} showed the presence of three NH groups. The absence of the peak in the region 2500–2400 cm^{-1} had revealed the presence of only C=S moiety and not the SH group. The ^1H NMR spectrum showed a multiplet at δ 1.25 which, was due to the methyl protons at C_3 position. The protons at C_3, C_{3a}, C_{5a}, C_{10a} and C_{10b} resonated as a multiplet between δ 1.30–2.17. An unresolved multiplet between δ 2.54–2.67 of two-proton intensity was due to the C_4 protons. The C_5 protons appeared as a multiplet in the region δ 2.76-3.19. The methyl protons at C_{10} were inferred as a singlet with three-proton intensity at δ 2.49. The N_1H proton also appeared as a multiplet between δ 5.23–5.27. The N_2H proton resonated as a multiplet between δ 6.05–6.19. The aromatic protons at C_6, C_7 and C_8 resonated as a cluster between the region of δ 7.04–7.64. The carbazole NH appeared as a multiplet centred at δ 8.77. The absence of the broad singlet in the region of δ 3.00 to 4.00 had confirmed that the SH group is not present in the compound. Further the molecular ion peak, *m/z* at 243 (29%) and the elemental analysis C: 74.15, H: 8.72 and N: 17.13% agreed well with the molecular formula, $C_{15}H_{21}N_3$. Based on the spectral data and the elemental analysis the



Scheme 2



Scheme 3

structure of the compound was found to be as 3,9-dimethyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-*a*]carbazole **4a**. The repeatability of the experiment was tested on **2b**–**e** to afford **4b**, **4c**, **4d** and **4e**, respectively (Scheme 1).

The plausible mechanism for the formation of **4** might be as follows. Hydrazine hydrate has been recognised to operate through different mechanistic modes depending on the functionality with which it chemically reacts.[22-24] The reagent may act both as condensing agent and as well as reducing agent. So it may reasonably be assumed that the hydrazine hydrate condenses with 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-one (**2**) followed by the nucleophilic attack cum cyclisation on β-carbon atom to afford the intermediate **10** which tautomerises to the intermediate **11.** This intermediate **11** on hydrogenation with the reagent[23,24] afforded the compound **4**.

In another typical experiment the reaction of 8-methyl-2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-one **2a** with thiourea in alcoholic KOH afforded a product which melted at 95 °C. The IR spectrum showed three strong bands at 3450, 3350, 3273 cm^{-1} corresponding to the NH group stretching vibrations. A prominent band at 1331 cm^{-1} was due to the C-N group stretching vibration. The C=S group appeared as a less intense band at 1175 cm^{-1}. The ^1H NMR spectrum showed a doublet centred at δ 1.99 with a three proton intensity and a *J* value of 7.42 Hz, which was due to the C_4-methyl group protons. The methylene protons at C_5 and C_6 appeared as two multiplets between δ 2.13–2.47 and δ 2.60–2.85, respectively. A doublet centred at δ 4.92 with *J* = 10.77 Hz was due to the C_3-NH proton. The C_4 proton appeared as a multiplet in the region δ 5.81–5.89 Hz. The methyl group protons at C_{10} resonated as a singlet δ 2.32. The aromatic proton at C_7 position appeared as a doublet centred at δ 7.23 with a *J* value of 8.00 Hz. The C_9 proton appeared as a doublet δ 7.41 with *J* = 8.10 Hz, respectively. The C_8 proton resonated as an unresolved multiplet between δ 7.52–7.73. The multiplet between δ 11.10–11.27 was due to the carbazole–NH and the C_1-NH protons. Though the molecular ion peak, *m/z* 283, did not appear in its mass spectrum, the appearance of the fragment ion peak at 249 (M^+-34) shows that, the sulfur group was eliminated as H_2S gas as normally observed in mercapto compounds.[22] The elemental analysis, C: 67.92; H: 06.10; N: 14.87 % and S: 11.25 supported well the proposed molecular formula, $C_{16}H_{17}N_3S$. The spectral data and the elemental analysis data augmented that the structure of the compound to be 4, 10-dimethyl-1,3,4,5,6,11-hexahydropyrimido[4,5-*a*]carbazole-2-thione **5a**. A similar series of compounds, **5b**–**e** were obtained by repeating the experiment with **2b**, **2c**, **2d** and **2e** (Scheme 1).

Experimental

General: Thin layer chromatography was used to access the purity of the products. Melting points were determined by using a Mettler FP 51 melting point apparatus and are uncorrected. IR spectra were recorded using KBr discs on a Shimadzu FTIR-8201 PC Infrared Spectrophotometer and ^1H NMR and ^{13}C NMR on a Varian AMX 400 FT-NMR spectrometer using TMS as internal reference in $CDCl_3$. The chemical shifts are quoted in parts per million. Mass spectra were recorded on a Joel JMS-D 300 mass spectrometer. Satisfactory microanalyses were obtained with Perkin Elmer Model 240 CHN analyser. Nomenclature of the hitherto prepared compounds is given in accordance with IUPAC rules for nomenclature of organic compounds.

*Reaction of 3,4-dihydrocarbazol-1(2H)-one **1** with dimethylcarbonate in presence of ethanol: General procedure:* In 10 ml of dry benzene 2.400 g of sodium hydride (degreased with low boiling petroleum ether) was added and kept on an ice bath. Dimethylcarbonate (6 ml) was added to sodium hydride with stirring. After 10 minutes a solution of the respective 3,4-dihydrocarbazol-1(2*H*)-one (**1**, 0.006 mol) in 20 ml of dry benzene was added and stirred under ice cold condition. To initiate the reaction 10 ml of absolute ethanol was added in drops to the above reaction mixture and the stirring was continued for 24 h. At the end of the period the excess of the solvent was removed by distillation. The reaction mixture was poured into ice cold water and neutralised with ice cold dilute HCl. Then the mixture was extracted with ethyl acetate and the organic layer was thoroughly washed with water. The organic layer was dried over anhydrous sodium sulphate, followed by the removal of the solvent. The reaction mixture yielded a brown crude product, which was purified by using column chromatography over silica gel. Petroleum ether and ethyl acetate mixture (98 : 2) was used as eluant to afford the corresponding 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-one **2** as yellow crystalline prisms.

8-Methyl-2-ethylidene-3,4-dihydrocarbazol-1(2H)-one (**2a**): M.p.: 160–162 °C; Mol. formula: $C_{15}H_{15}NO$; Yield: 80% (1.080 g); M. Wt.: 225.15; Calcd (%): C, 80.01; H, 6.66; N, 6.22; Found (%): C, 80.09; H, 6.59; N, 6.28; IR (KBr, ν_{max} cm^{-1}): 3283, 2925, 2857, 1659, 1601, 1547, 1477, 1377, 1329, 1298; ^1H NMR ($CDCl_3$, δ ppm): 1.93 (d, 3H, C_2=CH–C**H$_3$**, *J* = 7.20 Hz), 2.50 (s, 3H, C_8–CH_3), 2.99–3.09 (m, 4H, C_3–2H, C_4–2H), 6.96 (q, 1H, C_2=C**H**–CH_3, *J* = 7.20 Hz), 7.05–7.10 (m, 1H, C_6–H), 7.17 (d, 1H, C_5–H, *J* = 7.00 Hz), 7.51 (d, 1H, C_7–H, *J* = 7.86 Hz), 8.91 (b s, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 14.02 (C_1–CH_3), 16.73 (C_8–CH_3), 20.97 (C_3), 21.57 (C_4), 25.50 (C_2), 38.28 ($C_{2'}$), 118.83 (C_5), 120.65 (C_7), 122.00 (C_6), 125.64 (C_8), 127.18 (C_{4b}), 129.29 (C_{4a}), 132.60 (C_{9a}), 138.33 (C_{8a}), 180.17 (C=O); MS (*m/z*): 225.

7-Methyl-2-ethylidene-3,4-dihydrocarbazol-1(2H)-one (**2b**): M.p.: 169–171 °C; Mol. formula: $C_{15}H_{15}NO$; Yield: 82% (1.107 g); M. Wt.: 225.15; Calcd (%): C, 80.01; H, 6.66; N, 6.22; Found (%): C, 80.15; H, 6.58; N, 6.31; IR (KBr, ν_{max} cm^{-1}): 3240, 2923, 2854, 1651, 1640, 1587, 1437, 1334, 1316, 1263; ^1H NMR ($CDCl_3$, δ ppm): 1.92 (d, 3H, C_2=CH–C**H$_3$**, *J* = 7.14 Hz), 2.48 (s, 3H, C_7–CH_3), 2.98–3.32 (m, 4H, C_3–2H, C_4–2H), 6.93 (d, 1H, C_5–H, *J* = 8.36 Hz), 6.98 (q, 1H, C_2=C**H**–CH_3, *J* = 7.14 Hz), 7.21 (s, 1H, C_8–H), 7.53 (d, 1H, C_6–H, *J* = 8.36 Hz), 9.02 (b s, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.17 (C_1–CH_3), 16.25 (C_7–CH_3), 21.02 (C_3), 21.94 (C_4), 25.43 (C_2), 38.75 ($C_{2'}$), 119.05 (C_5), 120.21 (C_8), 122.73 (C_6), 125.91

(C_7), 128.14 (C_{4b}), 130.01 (C_{4a}), 132.35 (C_{9a}), 138.54 (C_{8a}), 181.85 (C=O); MS (*m/z*): 225.

6-Methyl-2-ethylidene-3,4-dihydrocarbazol-1(2H)-one (**2c**): M.p.: 192–194 °C; Mol. formula: $C_{15}H_{15}NO$; Yield: 78% (1.053 g); M. Wt.: 225.15; Calcd (%): C, 80.01; H, 6.66; N, 6.22; Found (%): C, 80.07; H, 6.61; N, 6.19; IR (KBr, ν_{max} cm^{-1}): 3238, 2925, 2854, 1655, 1637, 1597, 1541, 1340, 1319, 1265; ^{1}H NMR ($CDCl_3$, δ ppm): 1.92 (d, 3H, C_2=CH–C**H$_3$**, *J* = 7.19 Hz), 2.45 (s, 3H, C_6–CH_3), 2.98–3.06 (m, 4H, C_3–2H, C_4–2H), 6.95 (q, 1H, C_2=C**H**–CH_3, *J* = 7.19 Hz), 7.19 (d, 1H, C_7–H, *J* = 8.50 Hz), 7.32 (d, 1H, C_8–H, *J* = 8.50 Hz), 7.42 (s, 1H, C_5–H), 9.01 (b s, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 14.77 ($C_{1'}$–CH_3), 16.51 (C_6–CH_3), 20.61 (C_3), 21.22 (C_4), 25.81 (C_2), 39.02 ($C_{2'}$), 119.15 (C_5), 121.17 (C_7), 123.02 (C_8), 125.76 (C_6), 128.15 (C_{4b}), 129.44 (C_{4a}), 132.92 (C_{9a}), 138.43 (C_{8a}), 183.12 (C=O); MS (*m/z*): 225.

2-Ethylidene-3,4-dihydrocarbazol-1(2H)-one (**2d**): M.p.: 187–190 °C; Mol. formula: $C_{14}H_{13}NO$; Yield: 85% (1.076 g); M. Wt.: 211.14; Calcd (%): C, 79.63; H, 6.16; N, 6.63; Found (%): C, 79.58; H, 6.21; N, 6.59; IR (KBr, ν_{max} cm^{-1}): 3390, 3250, 2923, 2854, 1652, 1591, 1541, 1475, 1387, 1335, 1263; ^{1}H NMR ($CDCl_3$, δ ppm): 1.93 (d, 3H, C_2=CH–C**H$_3$**, *J* = 7.20 Hz), 2.92–3.08 (m, 4H, C_3–2H, C_4–2H), 6.97 (q, 1H, C_2=C**H**–CH_3, *J* = 7.20 Hz), 7.13–7.18 (m, 1H, C_6–H), 7.34–7.41 (m, 1H, C_7–H), 7.43 (d, 1H, C_5–H, *J* = 8.28 Hz), 7.66 (d, 1H, C_8–H, *J* = 7.92 Hz), 9.10 (b s, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.91 ($C_{1'}$–CH_3), 20.44 (C_3), 21.81 (C_4), 25.36 (C_2), 38.95 ($C_{2'}$), 118.29 (C_5), 121.67 (C_7), 122.47 (C_6), 123.17 (C_8), 128.74 (C_{4b}), 129.81 (C_{4a}), 133.19 (C_{9a}), 138.69 (C_{8a}), 180.11 (C=O); MS (*m/z*): 211.

6-Chloro-2-ethylidene-3,4-dihydrocarbazol-1(2H)-one (**2e**): M.p.: 170–172 °C; Mol. formula: $C_{14}H_{12}NOCl$; Yield: 75% (1.103 g); M. Wt.: 245.14; Calcd (%): C, 68.46; H, 4.89; N, 6.51; Found (%): C, 68.50; H, 4.83; N, 6.47; IR (KBr, ν_{max} cm^{-1}): 3236, 2925, 2857, 1655, 1601, 1541, 1466, 1385, 1319; ^{1}H NMR ($CDCl_3$, δ ppm): 1.93 (d, 3H, C_2=CH–C**H$_3$**, *J* = 7.24 Hz), 2.93–3.03 (m, 4H, C_3–2H, C_4–2H), 6.97 (q, 1H, C_2=C**H**–CH_3, *J* = 7.24 Hz), 7.29–7.45 (m, 2H, C_7–H, C_8–H), 7.63 (s, 1H, C_5–H), 9.26 (b s, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.78 ($C_{1'}$–CH_3), 20.47 (C_3), 21.25 (C_4), 25.79 (C_2), 39.09 ($C_{2'}$), 119.27 (C_5), 121.09 (C_7), 123.15 (C_8), 127.16 (C_6), 128.57 (C_{4b}), 129.81 (C_{4a}), 133.17 (C_{9a}), 138.51 (C_{8a}), 181.78 (C=O); MS (*m/z*): 245.

Synthesis of 3-methyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-a]carbazoles **4**: *General procedure:* The respective 2-ethylidene-3,4-dihydrocarbazol-1(2*H*)-one (**2**, 0.001 mol) and hydrazine hydrate (0.02 mol) was dissolved in dry ethanol and the resulting mixture was refluxed on a water bath for 5 h. After the reaction period, the excess of ethanol was removed by distillation and poured into crushed ice. The reaction mixture was extracted with ethyl acetate and washed with water. The organic layer was dried over anhydrous sodium sulphate. On removal of solvent, it yielded a white powder which was further purified by recrystallisation using petroleum ether : ethyl acetate mixture (90:10) to obtain the respective, 3-methyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-a]carbazoles **4**.

3,9-Dimethyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-a]carbazole (**4a**): M.p.: 95–98 °C; Mol. formula: $C_{15}H_{21}N_3$; Yield: 75% (0.183 g); M. Wt.: 243.15; Calcd (%): C, 74.09; H, 8.64; N, 17.27; Found (%): C, 74.15; H, 8.72; N, 17.13; IR (KBr, ν_{max} cm^{-1}): 3490, 3410, 3277, 2924, 2854, 1637, 1618, 1544, 1535, 1438, 1377, 1328; ^{1}H NMR ($CDCl_3$, δ ppm): 1.25 (m, 3H, C_3–CH_3), 1.30–2.17 (m, 5H, C_3–H, C_{3a}–H, C_{5a}–H, C_{10a}–H, C_{10b}–H), 2.49 (s, 3H, C_9–CH_3), 2.54–2.67 (m, 2H, C_4–2H), 2.76–3.19 (m, 2H, C_5–2H), 5.23–5.27 (m, 1H, pyrazolino-N_1H), 6.05–6.19 (m, 1H, pyrazolino-N_2H), 7.04–7.64 (m, 3H, C_6–H, C_7–H, C_8–H), 8.65–8.90 (m, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.60 (C_3–CH_3), 16.64 (C_9–CH_3), 20.96 (C_{3a}), 22.51 (C_4), 22.71 (C_5), 25.94 (C_{10a}), 29.72 (C_{5a}), 32.17 (C_{10b}), 35.94 (C_3), 119.01 (C_7), 120.74 (C_6), 121.87 (C_8), 125.56 (C_9), 126.01 (C_{9a}), 136.13 (C_{5b}); MS (*m/z*): 243.

3,8-Dimethyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-a]carbazole (**4b**): M.p.: 83–85 °C; Mol. formula: $C_{15}H_{21}N_3$; Yield: 78% (0.190 g); M. Wt.: 243.15; Calcd (%): C, 74.09; H, 8.64; N, 17.27; Found (%): C, 74.01; H, 8.59; N, 17.40; IR (KBr, ν_{max} cm^{-1}): 3450, 3280, 3090, 2923, 2853, 1649, 1625, 1543, 1466, 1376, 1328; ^{1}H NMR ($CDCl_3$, δ ppm): 1.25 (m, 3H, C_3–CH_3), 1.30–2.17 (m, 5H, C_3–H, C_{3a}–H, C_{5a}–H, C_{10a}–H, C_{10b}–H), 2.47 (s, 3H, C_8–CH_3), 2.24–2.38 (m, 2H, C_4–2H), 2.53–3.30 (m, 2H, C_5–2H), 5.22–5.53 (m, 1H, pyrazolino-N_1H), 6.11–6.14 (m, 1H, pyrazolino-N_2H), 6.85–7.56 (m, 3H, C_6–H, C_7–H, C_8–H), 8.60–9.05 (m, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.27 (C_3–CH_3), 16.91 (C_8–CH_3), 21.07 (C_{3a}), 22.19 (C_4), 23.01 (C_5), 26.10 (C_{10a}), 29.58 (C_{5a}), 32.48 (C_{10b}), 36.05 (C_3), 120.15 (C_7), 121.01 (C_6), 122.31 (C_9), 125.79 (C_9), 127.09 (C_{9a}), 136.77 (C_{5b}); MS (*m/z*): 243.

3,8-Dimethyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino[4,5-a]carbazole (**4c**): M.p.: 102–105 °C; Mol. formula: $C_{15}H_{21}N_3$; Yield: 72% (0.175 g); M. Wt.: 243.15; Calcd (%): C, 74.09; H, 8.64; N, 17.27; Found (%): C, 74.15; H, 8.60; N, 17.25; IR (KBr, ν_{max} cm^{-1}): 3495, 3375, 3248, 2924, 2855, 1667, 1633, 1599, 1545, 1375, 1340, 1319, 1292; ^{1}H NMR ($CDCl_3$, δ ppm): 1.26 (m, 3H, C_3–CH_3), 1.30–2.17 (m, 5H, C_{1a}–H, C_3–H, C_{3a}–H, C_{5a}–H, C_{10a}–H), 2.45 (s, 3H, C_7–CH_3), 2.27–2.30 (m, 2H, C_4–2H), 2.52–3.00 (m, 2H, C_5–2H), 5.26–5.29 (m, 1H, pyrazolino-N_1H), 6.13–6.19 (m, 1H, pyrazolino-N_2H), 7.08–7.52 (m, 3H, C_6–H, C_8–H, C_9–H), 8.51–8.67 (m, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.41 (C_3–CH_3), 17.04 (C_7–CH_3), 21.01 (C_{3a}), 22.32 (C_4), 22.89 (C_5), 26.05 (C_{10a}), 29.17 (C_{5a}), 32.99 (C_{10b}), 35.78 (C_3), 119.62 (C_6), 121.05 (C_8), 123.02 (C_9), 125.41 (C_7), 126.81 (C_{9a}), 138.54 (C_{5b}); MS (*m/z*): 243.

1,2,3,3a,4,5,5a,10,10a,10b-Decahydropyrazolino[4,5-a]carbazole (**4d**): M.p.: 110–113 °C; Mol. formula: $C_{14}H_{19}N_3$; Yield: 78% (0.179 g); M. Wt.: 229.14; Calcd (%): C, 73.30; H, 8.29; N, 18.23; Found (%): C, 73.30; H, 8.35; N, 18.39; IR (KBr, ν_{max} cm^{-1}): 3410, 3390, 3265, 2925, 2853, 1654, 1637, 1618, 1541, 1508, 1370, 1327; ^{1}H NMR ($CDCl_3$, δ ppm): 1.24 (m, 3H, C_3–CH_3), 1.40–2.17 (m, 5H, C_{1a}–H, C_3–H, C_{3a}–H, C_{5a}–H, C_{10a}–H), 2.21–2.39 (m, 2H, C_4–2H), 2.26–3.07 (m, 2H, C_5–2H), 4.36–4.80 (m, 1H, pyrazolino-N_1H), 5.05–5.22 (m, 1H, pyrazolino-N_2H), 7.06–7.11 (m, 4H, C_6–H, C_7–H, C_8–H, C_9–H), 10.73–11.59 (m, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.89 (C_3–CH_3), 21.05 (C_{3a}), 23.19 (C_4), 23.81 (C_5), 25.67 (C_{10a}), 29.14 (C_{5a}), 32.86 (C_{10b}), 36.07 (C_3), 120.01 (C_7), 120.78 (C_6), 121.55 (C_8), 122.01 (C_9), 126.42 (C_{9a}), 138.31 (C_{5b}); MS (*m/z*): 229.

7-Chloro-3-methyl-1,2,3,3a,4,5,5a,10,10a,10b-decahydropyrazolino [4,5-a]carbazole (**4e**): M.p.: 141–143 °C; Mol. formula: $C_{14}H_{18}N_3Cl$; Yield: 70% (0.184 g); M. Wt.: 263.14; Calcd (%): C, 63.79; H, 06.83; N, 15.93; Found (%):C, 63.71; H, 06.90; N, 15.86; IR (KBr, ν_{max} cm^{-1}): 3456, 3370, 3240, 2926, 2855, 1657, 1632, 1610, 1560, 1545, 1381, 1317; ^{1}H NMR ($CDCl_3$, δ ppm): 1.26 (m, 3H, C_3–CH_3), 1.31–2.18 (m, 5H, C_{1a}–H, C_3–H, C_{3a}–H, C_{5a}–H, C_{10a}–H), 2.24–2.34 (m, 2H, C_4–2H), 2.86–3.03 (m, 2H, C_5–2H), 5.22–5.28 (m, 1H, pyrazolino-N_1H), 6.11–6.19 (m, 1H, pyrazolino-N_2H), 7.17–7.62 (m, 3H, C_6–H, C_8–H, C_9–H), 8.85–9.10 (b s, 1H, carbazole–NH); ^{13}C NMR ($CDCl_3$, δ ppm): 15.91 (C_3–CH_3), 21.58 (C_{3a}), 22.87 (C_4), 22.91 (C_5), 26.61 (C_{10a}), 29.37 (C_{5a}), 33.10 (C_{10b}), 35.12 (C_3), 120.01 (C_6), 121.79 (C_8), 123.56 (C_9), 125.83 (C_7), 126.18 (C_{9a}), 138.48 (C_{5b}); MS (*m/z*): 263.

Synthesis of 4-methyl-1,3,4,5,6,11-hexahydropyrimido[4,5-a]carbazole-2-thiones **5**: *General procedure*: The appropriate 2-ethylidene-3,4-dihydrocarbazol-1(2H)-one (**2**, 0.001 mol) was dissolved in 4% alcoholic KOH solution. To this mixture thiourea (0.002 mol) was added and refluxed on a water bath for 6 h. The excess of ethanol was removed. The reaction mixture was then poured into crushed ice and the solid separated was filtered washed, dried and recrystallised using petroleum ether-ethyl acetate (85 : 15) to afford 4-methyl-1,3,4,5,6,11-hexahydropyrimido[4,5-a]carbazole-2-thione **5** as yellow prisms.

4,10-Dimethyl-1,3,4,5,6,11-hexahydropyrimido[4,5-a]carbazole-2-thione (**5a**): M.p.: 92–95 °C; Mol. formula: $C_{16}H_{17}N_3S$; Yield: 82% (0.232 g); M. Wt.: 283.23; Calcd (%): C, 67.85; H, 6.00; N, 14.83, S 11.32; Found (%): C, 67.92; H, 6.10; N, 14.87, S, 11.25; IR (KBr, ν_{max} cm^{-1}): 3450, 3350, 3273, 2922, 2856, 2345, 1645, 1611, 1553, 1475, 1331, 1175, 1142; ^{1}H NMR (DMSO–d_6, δ ppm): 1.99 (d, 3H, C_4–CH_3, *J* = 7.24 Hz), 2.13–2.47 (m, 2H, C_5–2H), 2.32 (s, 1H, C_{10}–CH_3), 2.60–2.85 (m, 2H, C_6–2H), 4.92 (d, 1H, pyrimido–N_3H, *J* = 10.77 Hz), 5.81–5.89 (m, 1H, C_4–H), 7.23 (d, 1H, C_7–H, *J* = 8.00 Hz), 7.41 (d, 1H, C_9–H, *J* = 8.10 Hz), 7.52–7.73 (m, 1H, C_8–H), 11.10–11.27 (m, 2H, carbazole–N_{11}H and pyrimido–N_1H); ^{13}C NMR (DMSO–d_6, δ ppm): 16.90 (C_4–CH_3), 18.46 (C_{10}–CH_3), 20.95 (C_5), 24.65 (C_6), 115.02 (C_{6a}), 118.45 (C_8), 119.84 (C_7), 120.02 (C_9), 122.38 (C_{10}), 125.85 (C_{4a}), 126.40 (C_{6b}), 137.16 (C_{11a}), 138.98 (C_{11b}), 193.14 (C=S); MS (*m/z*): 249 (M^+-34).

4,9-Dimethyl-1,3,4,5,6,11-hexahydropyrimido[4,5-a]carbazole2-thione (**5b**): M.p.: 120–125 °C; Mol. formula: $C_{16}H_{17}N_3S$; Yield: 85% (0.241 g); M. Wt.: 283.23; Calcd (%): C, 67.85; H, 6.00; N, 14.83, S 11.32; Found (%): C, 67.79; H, 5.83; N, 14.89, S, 11.36; IR (KBr, ν_{max} cm^{-1}): 3410, 3325, 3270, 2922, 2853, 1640, 1612, 1560, 1508, 1340, 1207; ^{1}H NMR (DMSO–d_6, δ ppm): 1.88 (d, 3H, C_4–CH_3, *J* = 7.00 Hz), 2.13–2.54 (m, 2H, C_5–2H), 2.62 (s, 3H, C_9–CH_3), 2.77–3.22 (m, 2H, C_6–2H), 5.16 (d, 1H, pyrimido–N_3H, *J* = 10.70 Hz), 6.05–6.12 (m, 1H, C_4–H), 7.04–7.53 (m, 2H, C_7–H and C_8–H), 7.56 (s, 1H, C_{10}–H), 11.22–11.64 (m, 2H, carbazole–N_{11}H

and pyrimido–N_1H); ^{13}C NMR (DMSO–d_6, δ ppm): 17.01 (C_4–CH_3), 18.95 (C_9–CH_3), 21.08 (C_5), 25.11 (C_6), 116.05 (C_{6a}), 119.59 (C_8), 120.01 (C_7), 120.39 (C_{10}), 123.95 (C_9), 126.77 (C_{4a}), 127.01 (C_{6b}), 137.47 (C_{10c}), 139.02 (C_{10b}), 192.77 (C=S); MS (*m*/*z*): 249 (M^+-34).

4,8-Dimethyl-1,3,4,5,6,11-hexahydropyrimido[4,5-a]carbazole-2-thione (**5c**): M.p.: 100–103 °C; Mol. formula: $C_{16}H_{17}N_3S$; Yield: 80% (0.226 g); M. Wt.: 283.23; Calcd (%): C, 67.85; H, 6.00; N, 14.83, S 11.32; Found (%): C, 67.93; H, 6.07; N, 14.78, S, 11.28; IR (KBr, ν_{max} cm^{-1}): 3450, 3320, 3285, 2924, 2855, 1643, 1611, 1541, 1438, 1377, 1292, 1184; ^{1}H NMR (DMSO–d_6, δ ppm): 1.88 (d, 3H, C_4–CH_3, *J* = 7.24 Hz), 2.13–2.56 (m, 2H, C_5–2H), 2.39 (m, 1H, C_8–CH_3), 2.81–3.07 (m, 2H, C_6–2H), 5.16 (d, 1H, pyrimido–N_3H, *J* = 10.70 Hz), 6.05–6.12 (m, 1H, C_4–H), 7.14 (d, 1H, C_9–H, *J* = 8.04 Hz), 7.32 (d, 1H, C_{10}–H, *J* = 8.04 Hz), 7.44 (s, 1H, C_7–H), 11.42–11.50 (m, 2H, carbazole–N_{11}H and pyrimido–N_1H); ^{13}C NMR (DMSO–d_6, δ ppm): 16.51 (C_4–CH_3), 19.57 (C_8–CH_3), 21.71 (C_5), 25.67 (C_6), 116.72 (C_{6a}), 119.22 (C_7), 121.21 (C_9), 122.44 (C_8), 123.57 (C_{10}), 125.77 (C_{4a}), 126.47 (C_{6b}), 126.89 (C_{10a}), 137.48 (C_{10c}), 139.05 (C_{10b}), 190.55 (C=S); MS (*m*/*z*): 249 (M^+-34).

4-Methyl-1,3,4,5,6,11-hexahydropyrimido[4,5-a]carbazole-2-thione (**5d**): M.p.: 108–110 °C; Mol. formula: $C_{15}H_{15}N_3S$; Yield: 85% (0.229 g); M. Wt.: 269.15; Calcd (%): C, 66.92; H, 5.57; N, 15.60, S 11.91; Found (%): C, 66.87; H, 5.62; N, 15.66, S, 11.86; IR (KBr, ν_{max} cm^{-1}3415, 3390, 3238, 2922, 2855, 1650, 1618, 1555, 1435, 1331, 1211, 1205; ^{1}H NMR (DMSO–d_6, δ ppm): 1.90 (d, 3H, C_4–CH_3, *J* = 7.25 Hz), 2.15–2.58 (m, 2H, C_5–2H), 2.86–3.09 (m, 2H, C_6–2H), 5.17 (d, 1H, pyrimido–N_3H, *J* = 10.72 Hz), 6.06–6.11 (m, 1H, C_4–H), 7.07 (d, 1H, C_7–H, *J* = 7.04 Hz), 7.22–7.58 (m, 2H, C_8–H, C_9–H), 7.67 (d, 1H, C_{10}–H, *J* = 7.92 Hz), 11.56–11.83 (m, 2H, carbazole–N_{11}H and pyrimido–N_1H); ^{13}C NMR (DMSO–d_6, δ ppm): 16.95 (C_4–CH_3), 21.15 (C_5), 25.77 (C_6), 116.01 (C_{6a}), 117.51 (C_8), 119.14 (C_7), 121.71 (C_9), 123.48 (C_{10}), 125.39 (C_{4a}), 126.40 (C_{6b}), 127.37 (C_{10a}), 138.21 (C_{10c}), 139.46 (C_{10b}), 194.05 (C=S); MS (*m*/*z*): 235 (M^+-34).

8-Chloro-4-methyl-13,4,5,6,11-hexahydropyrimido[4,5-a] carbazole-2-thione (**5e**): M.p.: 118–120 °C; Mol. formula: $C_{15}H_{14}N_3SCl$; Yield: 79% (0.239 g); M. Wt.: 303.23; Calcd (%): C, 59.32; H, 4.61; N, 13.83, S 10.56; Found (%): C, 59.38; H, 4.54; N, 13.75, S, 10.31; IR (KBr, ν_{max} cm^{-1}): 3410, 3390, 3277, 2924, 2853, 1657, 1607, 1560, 1468, 1329, 1275, 1207; ^{1}H NMR (DMSO–d_6, δ ppm): 1.89 (d, 3H, C_4–CH_3, *J* = 7.32 Hz), 2.15–2.59 (m, 2H, C_5–2H), 2.82–3.09 (m, 2H, C_6–2H), 5.18 (d, 1H, pyrimido–N_3H, *J* = 10.71 Hz), 6.09–6.13 (m, 1H, C_4–H), 7.19–7.34 (m, 1H, C_9–H), 7.40–7.52 (m, 1H, C_{10}–H), 7.67 (s, 1H, C_7–H), 11.77–12.05 (m, 2H, carbazole–N_{11}H and pyrimido–N_1H); ^{13}C NMR (DMSO–d_6, δ ppm): 16.87 (C_4–CH_3), 21.44 (C_5), 25.79 (C_6), 117.18 (C_{6a}), 119.12 (C_7), 121.23 (C_9), 122.78 (C_8), 124.09 (C_{10}), 125.36 (C_{4a}), 126.68 (C_{6b}), 127.11 (C_{10a}), 137.99 (C_{10c}), 138.81 (C_{10b}), 193.04 (C=S); MS (*m*/*z*): 269 (M^+-34).

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