Utility of 1-oxo-1,2,3,4-tetrahydrocarbazoles and 1-hydroxycarbazoles

3.1. Synthesis of 1-N,N-diacetylaminocarbazoles

Nitrogen containing heterocycles bearing amino substituents are of broad pharmaceutical interest\textsuperscript{109,227-229} that justifies continuing efforts in the development of structure activity relationship of novel compounds in this series of new synthetic strategies. Therapeutical prominences of carbazole derivatives are well established. In particular, these alkaloids show definite antitumour characteristics and have good prospects for future medicinal use. However, a major drawback in using these classes of compounds as drugs is their notorious insolubility in water, which makes it extremely difficult to administer the drug in intravenous form, severely limiting its practical potential and possible use. Incorporation of amino group into these systems will enhance the hydrophilicity of the molecule and therefore enhances its water solubility.\textsuperscript{228} It is well known that the presence of an amino group in the N-position of the indole nucleus shows much promise as a rehabilitative drug for the Alzheimer's disease\textsuperscript{230} and therefore the aminocarbazole derivatives have potential in being significantly active to both Alzheimer's disease and cancer. The antiproliferative activities of these compounds have been reported as being related to its high DNA binding affinity. Among the steric constraints that control this interaction, the presence of alkyl amino substitutions on the molecule is certainly important as far as drug DNA binding is concerned.\textsuperscript{231} Keeping these facts in mind, we aimed to derive hitherto unknown 1-(5-spiro-4-acetyl-2-amino-\Delta^2-1,3,4-thiadiazoline)-1,2,3,4-tetrahydrocarbazoles from the corresponding 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles upon cyclisation with acetic anhydride followed by hydrolysis.

\[ \text{R} = \text{H, CH}_3, \text{Cl} \]
Our expectation was based on an analogous situation in which the transformation of 2,6-diphenyl-4-thiosemicarbazonopiperidine to N-acetyl-2,6-diphenylpiperidine-4-yl-5-spiro-4-acetyl-2-(acetylamino)-Δ^2-1,3,4-thiadiazoline was effected using acetic anhydride.\(^{23a}\)

To realize our objective, 1-oxo-1,2,3,4-tetrahydrocarbazoles (1a-e) upon reaction with thiosemicarbazide hydrochloride in ethanol furnished 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles (2a-e), which upon reaction with acetic anhydride gave 1-N,N-diacetylaminocarbazoles (4a-e) instead of expected spiro compounds (Scheme 3.1). The structures of all the compounds were determined based on their spectroscopic and analytical data. The reaction mechanism for the formation of 1-N,N-diacetylaminocarbazoles has also been explained (Scheme 3.2).

**Scheme 3.1**

1-4

**1.** \(R_1 = R_2 = R_3 = H\)

**2.** \(R_1 = \text{CH}_3, R_2 = R_3 = H\)

**3.** \(R_2 = \text{CH}_3, R_1 = R_3 = H\)

**4.** \(R_3 = \text{CH}_3, R_1 = R_2 = H\)

**5.** \(R_1 = \text{Cl}, R_2 = R_3 = H\)
The synthon, 1-oxo-1,2,3,4-tetrahydrocarbazole (1a) upon reaction with thiosemicarbamide hydrochloride in ethanol yielded 90% of 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a). Its IR spectrum (Fig 1) showed strong absorption bands at 3440 cm\(^{-1}\) (CS\(\text{NH}_2\)), 3300 (indole NH), 3145 cm\(^{-1}\) (NHCS) and 1577 cm\(^{-1}\) (C=\(\text{N}\)). Its \(^1\)H NMR spectrum (Fig 2) displayed a pentet at \(\delta\) 1.93-1.96 and two multiplets at \(\delta\) 2.69-2.73 and \(\delta\) 2.75-2.78 correspond to C\(_3\), C\(_2\) and C\(_4\) methylene protons respectively. The aromatic region showed well-defined signals as two doublets and two triplets at \(\delta\) 7.49 (J=8.00 Hz), \(\delta\) 7.32 (J=8.00 Hz), \(\delta\) 7.16 (J=7.58 Hz) and \(\delta\) 6.99 (J=7.58 Hz) for C\(_5\), C\(_8\), C\(_7\) and C\(_6\) aromatic protons respectively. The NH\(_2\) protons appeared as a singlet at \(\delta\) 8.29 and the two NH protons resonate at \(\delta\) 10.47 (ring NH) and at \(\delta\) 11.20 (NHCS). Mass spectrum exhibited molecular ion peak at m/z 258 (71%) and the base peak at m/z 183 [M\(^+\) - NHCS\(\text{NH}_2\)]. Further, the elemental analysis C 60.53%, H 05.29%, N 21.68% was compatible well with the proposed molecular formula C\(_{15}\)H\(_{14}\)N\(_4\)S augmenting the structure of the product as 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a). A similar treatment when extended to 1b, 1c, 1d and 1e furnished the corresponding 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles 2b, 2c, 2d and 2e.

After obtaining the key intermediate, 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a), it was treated with acetic anhydride. After workup, it yielded a single product in quantitative yield melting at 128°C. The IR spectrum (Fig 3) showed the appearance of NH stretching frequency at 3350 cm\(^{-1}\) and carbonyl stretching frequency at 1680 cm\(^{-1}\). Its \(^1\)H NMR spectrum (Fig 4) displayed two singlets of three proton intensity at \(\delta\) 2.29 and \(\delta\) 2.43, three doublets of one proton intensity at \(\delta\) 7.48 (J=8.00 Hz), \(\delta\) 7.82 (J=8.00 Hz), \(\delta\) 7.97 (J=8.00 Hz), and two triplets of one proton intensity at \(\delta\) 7.01 (J=7.92 Hz), \(\delta\) 7.21 (J=7.92 Hz) in the aromatic region and a two proton multiplet in the region \(\delta\) 7.30-7.34. A broad singlet at \(\delta\) 8.79 corresponds to one proton intensity. The mass spectrum of the compound showed molecular ion peak at m/z 266 and elemental analysis C 72.25%, H 05.22%, N 10.69% were in good agreement with the proposed molecular formula C\(_{16}\)H\(_{14}\)N\(_2\)O\(_2\). Based on the above spectral and analytical data the product was identified as 1-N,N-diacetylaminocarbazole (4a). The scope of the reaction was successfully tested with other 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles 2b, 2c, 2d,
Fig 1. IR spectrum of 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a)

Fig 2. $^1$H NMR spectrum of 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a)
Fig 3. IR spectrum of 1-N,N-diacetylamincarbazole (4a)

Fig 4. $^1$H NMR spectrum of 1-N,N-diacetylamincarbazole (4a)
and 2e (Scheme 3.1). In all the cases, the corresponding series of compounds 4b, 4c, 4d and 4e were neatly obtained and characterized by analytical and spectral data.

In order to study the generality, the same reaction was extended to 1-semicarbazono-1,2,3,4-tetrahydrocarbazoles (3a-e) and similar products (4a-e) were obtained in all cases. Its \(^1\)H NMR, IR, mass, elemental analyses and mixed melting points were found to be identical with the product obtained from 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles (2a-e) (Scheme 3.1).

A plausible mechanism for the conversion of 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles (2) to 1-N,N-diacetylaminocarbazoles (4) was presented in scheme 3.2. 1-Thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2) tautomerises first to an intermediate I, then O-acylate with acetic anhydride to give the intermediate II and N-acetyl thiourea. The intermediate II on 3,3-sigmatropic rearrangement afforded 2-oxyacetyl intermediate III. Further, acetylation of III at the nitrogen atom gave IV, which loses acetic acid molecule to yield the intermediate V. This on aromatisation followed by acetylation at the nitrogen atom of amide VI to yield the final product 4.

Scheme 3.2
All the newly synthesized compounds were screened for their *in vitro* antibacterial activities against *Bacillus subtilis*, *Salmonella typhi*, *Aeromonas hydrophila*, *Escherischia coli*, and *Staphiloccus aureus* by disc diffusion method. The minimum inhibitory concentration (MIC values) was determined by serial dilution method. The results were tabulated below.

The antibacterial screening studies indicate that 1-N,N-diacylaminocarbazole carrying chloro group at sixth position (4e) showed excellent antibacterial activity against *Bacillus subtilis*, *Staphilococcus aureus* and *Aeromonas hydrophila*. Compound 4a also possessed good antibacterial activity against *Bacillus subtilis*, *Staphilococcus aureus* and *Staphillococcus aureus*.

### Antibacterial activity of 1-N,N-diacylaminocarbazoles (4)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Minimum inhibitory concentration /μg / mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>B. subtilis</em></td>
</tr>
<tr>
<td>4a</td>
<td>15</td>
</tr>
<tr>
<td>4b</td>
<td>50</td>
</tr>
<tr>
<td>4c</td>
<td>50</td>
</tr>
<tr>
<td>4d</td>
<td>50</td>
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<tr>
<td>4e</td>
<td>10</td>
</tr>
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3.2. Synthesis of 3,4-dihydro-2-thienyloxeteno[2,3-a]carbazoles

Heterocyclic compounds containing carbazole moiety have received considerable attention due to its therapeutic prominence. A large number of reports are available on the synthesis of tetracyclic pyridocarbazoles, yet other tetracyclic carbazole derivatives remain much unexplored. As well, pyrimidine bases containing oxetane ring in their side chain exhibit antiviral properties. So, it seems worthwhile to devise a simple synthetic route for a heterocyclic system containing both carbazole and oxetane nuclei along with thienyl substitution with an expectation to elicit interesting pharmacological activities, as they incorporate nitrogen, oxygen and sulphur atoms in their structure.

In this connection, 1-oxo-1,2,3,4-tetrahydrocarbazole (Ia) was subjected to mixed aldol condensation with thiophene-2-carboxaldehyde in 4% alc potassium hydroxide solution to yield 2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5a).

The structure of the product was proved by their analytical and spectral data. In its IR spectrum (Fig 5) the shift in the carbonyl absorption (1635 cm\(^{-1}\)) indicated the formation of \(\alpha,\beta\)-unsaturated carbonyl group. In its \(^1\)H NMR spectrum (Fig 6) the disappearance of C2 protons signal and the appearance of thienylic proton signal as a singlet at \(\delta 7.80\) proved the mixed aldol condensation of Ia with thiophene-2-carbaldehyde. The aromatic protons appeared as a multiplet at \(\delta 7.25-7.63\). Two multiplets at \(\delta 3.02\) and \(\delta 3.26\) correspond to C3-2H and C4-2H protons respectively. A broad singlet at \(\delta 9.21\) was due to NH proton. Further, the elemental analysis and mass spectrum confirmed the above structure. The mass spectrum of the product exhibited the molecular ion peak at m/z 279 (21%) and the
Fig 5. IR spectrum of 1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5a)

Fig 6. $^1$H NMR spectrum of 1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5a)
base peak at m/z 29. These details attest the structure 2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole 5a for the compound realized. The same synthetic strategy was extended to other 1-oxo-1,2,3,4-tetrahydrocarbazoles (1b-e) and in all the cases, the corresponding 2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (5b-e) were neatly obtained and characterized by analytical and spectral data (Scheme 3.3).

Many interesting reports have appeared on the synthesis of oxygen heterocyclic compounds by photocyclisation. As 2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5a) was an α,β-unsaturated ketone with thiophene group extending the conjugation furthermore, it is likely to be photosensitive. Hence, it was irradiated with UV light of wavelength 253.7 nm under non-oxidative conditions in sodium-dried benzene for 36 h. This yielded yellow crystalline powder. The absorptions in IR spectrum (Fig 7), at 3250 cm\(^{-1}\) and 1270 cm\(^{-1}\) were ascribable to NH and C-O-C stretchings respectively. Its \(^1\)H NMR spectrum (Fig 8) displayed multiplets at δ 3.09-3.19 and δ 3.38-3.40 (C3-2H and C4-2H), a singlet at δ 6.95 (olefinic-H), seven protons aromatic envelop at δ 7.05-7.69 and a broad singlet at δ 8.90 (-NH). It was pertinent to mention here that C2=CH proton appeared at downfield, δ 6.95 owing to its synchronous nature of being an allylic and olefinic proton. Moreover, it is at an α position to an electronegative oxygen atom of oxetane ring. The appearance of molecular ion peak at m/z 279 and elemental analysis agreed well with the proposed molecular formula C\(_{17}\)H\(_{13}\)NOS. On the basis of the above mentioned spectral and analytical data the structure was elucidated as 2-thienyl-3,4-dihydrooxeteno[2,3-a]carbazole (6a). Applicability of the above reaction was successfully tested with 5b, 5c, 5d and 5e (Scheme 3.4).

![Scheme 3.4](image)

5, 6a: R\(_1\) = R\(_2\) = R\(_3\) = H  
b: R\(_1\) = CH\(_3\), R\(_2\) = R\(_3\) = H  
c: R\(_2\) = CH\(_3\), R\(_1\) = R\(_3\) = H  
d: R\(_3\) = CH\(_3\), R\(_1\) = R\(_2\) = H  
e: R\(_1\) = Cl, R\(_2\) = R\(_3\) = H

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Fig 7. IR spectrum of 2-thienyl-3,4-dihydrooxeteno[2,3-α]carbazole (6a)

Fig 8. $^1$H NMR spectrum of 2-thienyl-3,4-dihydrooxeteno[2,3-α]carbazole (6a)
3.3. Synthesis of 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazoles and 4-phenyl-1H-3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazoles

The foregoing results that have emanated from our synthetic investigations on 1-oxo-1,2,3,4-tetrahydrocarbazoles were of considerable interest. It prompted us to focus our attention towards the construction of pyrazole and pyrimidine rings on carbazole skeleton. Interest in such compounds has been heightened by the discovery of pyridocarbazole an appropriate skeleton to design DNA intercalating drugs.56 Besides this, many tetracyclic compounds have been synthesized by the replacement of pyridine ring by other heterocyclic rings and to study their effects on their biological properties.174,175,177,232,241-244 Pyrimidine derivatives were found to possess variety of pharmacological activities.245 Pyrazoles were found wide applications in drugs, dyes and as anesthetics. Pyrazoles have also been used as antioxidants in fuels, but their major applications have been in medical and agricultural fields245a. Hence, it was contemplated to derive a facile route for pyrazolino and pyrimidocarbazoles by replacement of pyridine ring in pyridocarbazoles utilizing 2-benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles as suitable precursors.

2-Benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (7) prepared according to our reported procedure246 upon reaction with hydrazine hydrate in acetic acid247 yielded 8 which was found to be 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazoles based on their spectral and analytical data (Scheme 3.5).

Scheme 3.5

Reaction of 2-benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (7a) with hydrazine hydrate in acetic acid gave a product which showed IR absorptions (Fig 9) at 3449 cm⁻¹,
1650 cm\(^{-1}\) and 1533 cm\(^{-1}\) and these were ascribable to stretching frequencies of NH, C=O of acetyl group and C=N respectively. The \(^1\)H NMR spectrum (Fig 10) of the product showed the disappearance of benzylic proton signal of 7a and the appearance of C3-H proton signal as a doublet at \(\delta\) 4.88 (J=10.4 Hz), which confirmed that 7a was converted to 8a. The multiplets in the region \(\delta\) 1.72, \(\delta\) 2.05, \(\delta\) 2.84, \(\delta\) 3.09 and \(\delta\) 3.36 accounting for five protons each of one proton intensity correspond to C3 proton, C4 and C5 methylene protons. A singlet at \(\delta\) 2.39 inferred the presence of acetyl group attached to the nitrogen atom in position 2. The nine protons aromatic cluster resonated as a multiplet in the region \(\delta\) 7.14-7.72. The NH proton appeared as a singlet at \(\delta\) 8.62. The mass spectrum exhibited molecular ion peak at m/z 329 (44.6\%) and base peak at m/z 286 (M-COCH\(_3\)). In the proton decoupled \(^13\)C NMR spectrum, two methylene carbon signals were observed at 21.58 and 28.89 ppm. The methyl carbon resonates at 22.67 and CH carbon resonates at 56.57, 67.45, 111.83, 119.89, 120.50, 125.19, 126.06, 126.80, 127.33, 127.70, 129.01, and 129.11 ppm. The carbonyl carbon resonates at 141.68 ppm. Further, the elemental analysis agreed well with the proposed molecular formula C\(_{21}\)H\(_{19}\)N\(_3\)O. Based on all the above details, the compound was attested to be 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-f]carbazole 8a. Similarly, its derivatives 8b-e were prepared from 7b-e under identical conditions.

As another point of interest, 2-benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (7a) was allowed to react with thiourea in presence of alc potassium hydroxide.\(^{248}\) It afforded 4-phenyl-1H-3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9a) (Scheme 3.6). The structure of the product was confirmed based on the spectral and analytical data. The IR spectrum (Fig 11) of 9a showed C=S stretching frequency at 1595 cm\(^{-1}\) and a broad NH stretching frequency at 3440 cm\(^{-1}\). Its \(^1\)H NMR spectrum (Fig 12) showed C5 and C6 methylene protons signal as multiplets at \(\delta\) 2.87 and at \(\delta\) 2.98. The C4-H proton appeared as a doublet at \(\delta\) 4.50 (J=8.76 Hz). Aromatic protons displayed a multiplet at \(\delta\) 6.92-7.69. A broad singlet at \(\delta\) 9.00 corresponds to carbazole NH. The molecular ion peak at m/z 331 in its mass spectrum and elemental analysis C 72.52\%, H 05.25\%, N 12.83\% agreed very well with the proposed molecular formula C\(_{20}\)H\(_{17}\)N\(_3\)S augmenting the structure of the
Fig 9. IR spectrum of 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-α]carbazole (8a)

Fig 10. $^1$H NMR spectrum of 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-α]carbazole (8a)
Fig 11. IR spectrum of 4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9a)

Fig 12. $^1$H NMR spectrum of 4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9a)
product as 4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole 9a. The generality of the reaction was verified successfully with 7b, 7c, 7d and 7e.

**Scheme 3.6**

\[
\begin{array}{c}
\text{H}_2\text{N}-\text{C} \rightleftharpoons \text{NH}_2 \\
\text{alc. KOH}
\end{array}
\]

7, 9 a: R₁ = R₂ = R₃ = H  
 b: R₁ = CH₃, R₂ = R₃ = H  
 c: R₂ = CH₃, R₁ = R₃ = H  
 d: R₃ = CH₃, R₁ = R₂ = H  
 e: R₁ = Cl, R₂ = R₃ = H

3.4. 4-Oxopyrano[2,3-a]carbazoles

Pyrano[3,2-a]carbazoles such as Grinimbine, Mupamine, Mahanimbine, Murrayanol and Mahanine were isolated from plant species of Rutaceae family.249 In particular, the alkaloids mahanimbine, murrayanol and mahanine were reported to posses mosquitocidal, antimicrobial, antiinflammatory and antioxidant activities.3,249 To our knowledge there is no report on the synthesis of 2-alkyl- or 2-aryl-4-oxopyrano[2,3-a]carbazoles. From biogenetic point of view, there exists a possibility for the formation of these compounds in the plant body; yet their isolation has not been reported. Hence, it needs further extensive search in plant material for their presence. Based on the above facts, it was felt to device a simple synthetic method for 2-alkyl- or 2-aryl- 4-oxopyrano[2,3-a]carbazoles in a view that these compounds may be isolated in future.


In this context, 1-hydroxycarbazoles 10 were condensed with 3,3-dimethylacryloyl chloride in presence of aluminium iodide in acetonitrile.250 It ends up with the formation of three products in each case on thin layer chromatography (TLC), which were separated by performing column chromatography using petroleum ether-ethyl acetate as eluant. The
two products obtained from (99:1) and (85:15) petroleum ether-ethyl acetate fractions were found to be identical in all respects with the known products 2-(3',3'-dimethyl acryloyl)-1-hydroxycarbazoles (11) and 2,2-dimethyl-2H,11H-indolo[3,2-h]chroman-4-ones (12) respectively (mp, mixed mp, ^1'H NMR and superimposable IR spectra). Acid catalysed cyclisation of 11 resulted in the formation of 12. This confirmed the structure 2-(3',3'-dimethylacryloyl)-1-hydroxycarbazoles 11 for the compound realized. The product obtained from (97:3) petroleum ether-ethyl acetate fraction in each case was found to be a new product and identified as 2,2-dimethyl-6-(3',3'-dimethylacryloyl)-2H,11H-indolo[3,2-h]chroman-4-one 13 on the basis of IR and ^1'H NMR and mass spectral analyses (Scheme 3.7).

(Scheme 3.7)

The IR absorptions (Fig 13) of the newly derived one 13b showed two strong >C=O stretching vibrations at 1632 cm\(^{-1}\) and at 1601 cm\(^{-1}\) and –NH stretching vibration at 3401 cm\(^{-1}\). When we scrutinized the ^1'H NMR spectrum (Fig 14) of 13b, the appearance of five singlets due to five methyl groups each of three proton intensity at δ 1.56, δ 1.57, δ 2.07, δ 2.25 and δ 2.56 and methylene protons signal at δ 2.94 confirmed the product was different from indolo chromanone 12b. The spectrum displayed a signal at δ 6.90 due to olefinic proton and two doublets at δ 7.39 (J=8.2 Hz) and δ 7.57 (J=8.2 Hz) due to C₃ and
C_{10} protons respectively. Two singlets at δ 7.51 and δ 7.85 correspond to C_7 and C_5 protons respectively. A broad singlet at δ 8.45 was ascribable to NH proton. The molecular ion peak in its mass spectrum with m/z 361 and the elemental analysis agreed well with the proposed molecular formula C_{23}H_{23}NO_3. Based on the above spectral and analytical data the product was attested the structure 2,2,8-trimethyl-6-(3',3'-dimethylacryloyl)-2H,11H-indolo[3,2-ii]chroman-4-one (13b). A similar series of compounds 13a, 13c, and 13d along with the respective known compounds (11a, 11c, 11d and 12a, 12c, 12d) were obtained from the respective 1- hydroxycarbazoles 10a, 10c, and 10d under identical conditions (Scheme 3.7).

3.4.2. An attempt to device synthetic route for 2-phenylpyrano[2,3-a]carbazoles – 4-oxo-2-phenylpyrano[2,3-a]carbazoles

In the next attempt to derive 2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (14), the intended precursor of 5,6-dihydro-2-phenylpyrano[2,3-a]carbazoles (15), 1-oxo-1,2,3,4-tetrahydrocarbazoles (I) were subjected to mixed aldol condensation with cinnamaldehyde. It yielded 2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (14), which were confirmed by their spectral and analytical data (Scheme 3.8). When 6-chloro-1-oxo-1,2,3,4-tetrahydrocarbazole 1e was condensed with cinnamaldehyde in presence of alc potassium hydroxide at room temperature, it yielded a single product (Scheme 3.8). The IR spectrum (Fig 15) showed two strong absorptions at 1637 cm\(^{-1}\) and at 3226 cm\(^{-1}\) due to >C=O and -NH stretching vibrations respectively.

Scheme 3.8

![Scheme 3.8](image)

1, 14, 15 a: R_1 = R_2 = R_3 = H  
b: R_1 = CH_3, R_2 = R_3 = H  
c: R_2 = CH_3, R_1 = R_3 = H  
d: R_3 = CH_3, R_1 = R_2 = H  
e: R_1 = Cl, R_2 = R_3 = H

a: hv 253.2 nm, H_3PO_4, H^+ / EtOH

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Fig 13. IR spectrum of 3,4-dihydro-2,2,8-trimethyl-6-(3,3-dimethylacryloyl)-2H-11H-indolo[3,2-b]chroman-4-one (13b)

Fig 14. $^1$H NMR spectrum of 2,2,8-trimethyl-6-(3,3-dimethylacryloyl)-2H-11H-indolo[3,2-b]chroman-4-one (13b)
The $^1$H NMR spectrum (Fig 16) revealed that it was none other than the desired 6-chloro-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole $14e$ and the absorptions were assigned below.

(i) two ‘2H’ multiplets at $\delta$ 3.08 and $\delta$ 3.17 ($C_3$-H$_2$ & $C_4$-H$_2$)

(ii) two ‘1H’ doublets at $\delta$ 7.03 and $\delta$ 7.18 with $J = 15.34$ Hz (olefinic protons)

(iii) ‘9H’ multiplet at $\delta$ 7.20-7.65 ($C_5$-H, $C_7$-H, $C_8$-H, $C_2$.6-H, and olefinic proton)

(iv) a ‘1H’ broad singlet at $\delta$ 8.96 (NH)

The same outcome leading to $14a$-$d$ were realized when $1a$-$d$ were condensed with cinnamaldehyde.

6-Chloro-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole $14e$ thus obtained was irradiated with UV light of wavelength 253.7 nm in sodium dried benzene$^{240}$ in an expectation to obtain 8-chloro-5,6-dihydro-2-phenylpyra[2,3-a]carbazole $15e$. Unfortunately, the expected cyclisation did not commence. Hence, cyclisation was tried with other cyclising agents such as conc sulphuric acid in ethanol, phosphorus oxychloride, which also did not yield fruitful results. The reason behind it may be due to the trans nature of the cinnamyl protons. At this stage, it was felt to condense cinnamic acid with 1-hydroxycarbazoles $10$ in presence of freshly fused finely powdered zinc chloride and phosphorus oxychloride$^{252}$ to synthesize 2-phenyl-4-oxopyrano[2,3-a]carbazoles $17$ (Scheme 3.9).

Thus 6-methyl-1-hydroxycarbazole $10b$ was reacted with cinnamic acid using freshly fused finely powdered zinc chloride and phosphorus oxychloride$^{252}$ (Scheme 3.9). After workup, it showed only one spot on tlc and was found to be 2-cinnamoyl-6-methyl-1-hydroxycarbazole $16b$. Its IR spectrum (Fig 17) showed $>$C=O, NH and –OH stretching frequencies at 1630, 3381 and 3420 cm$^{-1}$ respectively. In its $^1$H NMR spectrum (Fig 18) the appearance of methyl protons signal at $\delta$ 2.53 and the aromatic cluster accounting for ten protons and two olefinic protons at $\delta$ 7.31–7.98 confirmed that cinnamic acid condensed with 6-methyl-1-hydroxycarbazole $10b$. The appearance of NH and OH signals at $\delta$ 8.50 and at $\delta$ 13.79 respectively, further confirmed that the product was an uncyclised
Fig 15. IR spectrum of 6-chloro-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14e).

Fig 16. $^1$H NMR spectrum of 6-chloro-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14e).
Fig 17. IR spectrum of 2-cinnamoyl-6-methyl-1-hydroxycarbazole (16b)

Fig 18. $^1$H NMR spectrum of 2-cinnamoyl-6-methyl-1-hydroxycarbazole (16b)
2-cinnamoyl-6-methyl-1-hydroxycarbazole 16b. Mass spectrum showed a molecular ion peak at m/z 327 (62%) and a base peak at m/z 223 by the loss of styrene molecule. Elemental analysis was in compatible with the molecular formula C\textsubscript{22}H\textsubscript{17}NO\textsubscript{2}. Based on the above spectral data the product was attested to be a 2-cinnamoyl-6-methyl-1-hydroxycarbazole 16b. A similar series of compounds 16a, 16c, and 16d were obtained form 10a, 10c and 10d respectively.

Scheme 3.9

2-Cinnamoyl-6-methyl-1-hydroxycarbazole 16b on oxidative cyclisation with DMSO in presence of catalytic amount of iodine for 10 min\textsuperscript{253} yielded the product 8-methyl-4-oxo-2-phenylpyrano[2,3-a]carbazole 17b. Its IR spectrum (Fig 19) showed strong absorptions at 3454 cm\textsuperscript{-1}, 1620 cm\textsuperscript{-1} (Shouldering starts at 1690 cm\textsuperscript{-1}) and at 1254 cm\textsuperscript{-1} corresponding to -NH, C=O and C-O-C stretching vibrations respectively. A sharp singlet at $\delta$ 2.49 in its $^1$H NMR spectrum (Fig 20) was due to the methyl group at C\textsubscript{8} carbon atom and a singlet in the downfield region at $\delta$ 7.11 corresponds to C\textsubscript{3}-H proton. The downfield shift was due to the deshielding effect of the phenyl ring at C\textsubscript{2} position. An aromatic envelop at $\delta$ 7.25–8.36 was consistent with ten aromatic protons and a broad singlet at $\delta$ 10.05 for the NH proton. Elemental analysis C 81.11%, H 04.79%, N 04.16% was in good agreement with the molecular formula C\textsubscript{22}H\textsubscript{15}NO\textsubscript{2}. On the basis of the above-
Fig 19. IR spectrum of 8-methyl-4-oxo-2-phenylpyrano[2,3-a]carbazole (17b)

Fig 20. $^1$H NMR spectrum of 8-methyl-4-oxo-2-phenylpyrano[2,3-a]carbazole (17b)
mentioned spectral evidence the product was assigned the structure 8-methyl-4-oxo-2-phenylpyrano[2,3-α]carbazole 17b. A series of similar compounds 17a, 17c and 17d were obtained from 10a, 10c and 10d through the intermediates 16a, 16c and 16d respectively (Scheme 3.9).

3.4.3. Synthesis of 2-methyl-4-oxopyrano[2,3-α]carbazoles

Among the carbazole derivatives ellipticine, 9-hydroxyellipticine,254 olivacine representing 3-aza analogs of pyrido[4,3-b]carbazoles, elicit high antitumour properties.36,37,157-160 Recently, a pyrido[4,3-α]carbazole was reported to show anti-HIV activity.40 Based on the above facts, it was worthwhile to device an elegant method for the synthesis of pyrido[2,3-α]carbazole derivatives and to evaluate their pharmacological activities. 1-Hydroxycarbazole (10) upon condensation with ethyl acetoacetate in presence of conc sulphuric acid afforded α-pyrone fused ring system with low yield.190 In this connection, 1-hydroxycarbazole 10 was condensed with ethyl acetoacetate in presence of zinc chloride and phosphorus oxychloride or with polyphosphoric acid with an expectation to afford α-pyrone fused ring system 18 from which 4-methyl-2-oxopyrido[2,3-α]carbazole (19) can be obtained by passing ammonia gas in alcoholic medium (Scheme 3.10).

Scheme 3.10

Thus, 6-methyl-1-hydroxycarbazole 10b was condensed with ethyl acetoacetate in presence of freshly fused finely powdered zinc chloride and phosphorus oxychloride or
with polyphosphoric acid. It yielded a single product. It did not give alcoholic ferric chloride test, which confirmed the absence of phenolic OH. The IR spectrum (Fig 21) also revealed the absence of hydroxyl group by lacking absorption around 3495 cm\(^{-1}\) (1-hydroxycarbazole) and the absence of lactone carbonyl around 1725 cm\(^{-1}\) (\(\alpha\)-pyrone) but documented the formation of C-O-C bond by exhibiting a strong band at 1258 cm\(^{-1}\) and \(\alpha,\beta\)-unsaturated C=O stretching vibration at 1646 cm\(^{-1}\). The \(^1\)H NMR spectrum (Fig 22) exhibited the following signals.

(i) two \(^3\)H singlets at \(\delta\) 2.53 and \(\delta\) 2.54 (C\(_2\)-CH\(_3\) & C\(_8\)-CH\(_3\))
(ii) a \(^1\)H singlet at \(\delta\) 6.58 (C\(_3\)-H)
(iii) two \(^1\)H doublets at \(\delta\) 6.98 and \(\delta\) 7.34 with \(J = 8.00\) Hz (C\(_9\)-H & C\(_5\)-H)
(iv) a \(^2\)H multiplet at \(\delta\) 7.24-7.28 (C\(_6\)-H & C\(_{10}\)-H)
(v) two \(^2\)H singlets at \(\delta\) 7.49 and \(\delta\) 7.83 (C\(_7\)-H & NH)

The mass spectrum of the compound exhibited an intense molecular ion peak at m/z 263 which itself was found to be the base peak. Elemental analysis was in agreement with the molecular formula C\(_{17}\)H\(_{13}\)N\(_2\). The above spectral data corresponds to compound 2,8-dimethyl-4-oxopyrano[2,3-a]carbazole (20b) and not 4,8-dimethyl-2-oxopyrano[2,3-a]carbazole (18b) (Scheme 3.10 and 3.11). Similar treatment of other 1-hydroxycarbazoles 10a, 10c and 10d gave corresponding 2-methyl-4-oxopyrano[2,3-a]carbazoles 20a, 20c and 20d (Scheme 3.11)

Scheme 3.11

1-Hydroxycarbazoles 10 upon condensation with ethyl acetoacetate in presence of conc sulphuric acid afforded \(\alpha\)-pyrone fused ring system\(^{100}\) but with zinc chloride and phosphorus oxychloride or with polyphosphoric acid, it gave a new system \(\gamma\)-pyrone fused
Fig 21. IR spectrum of 2,8-dimethyl-4-oxopyrano[2,3-α]carbazole (20b)

Fig 22. $^1$H NMR spectrum of 2,8-dimethyl-4-oxopyrano[2,3-α]carbazole (20b)
ring system, 2-methyl-4-oxopyrano[2,3-a]carbazoles 20 in moderate yields (Scheme 3.10). The structure of the product was confirmed based on the spectral and analytical data. Ethyl acetoacetate exists in both keto and enol forms. The enol form of ethyl acetoacetate condenses with the OH group of 1-hydroxycarbazole 10 to give 2-methyl-4-oxopyrano[2,3-a]carbazole 20. Despite the moderate yield, this reaction provides a short synthetic pathway to prepare 2-methyl-4-oxopyrano[2,3-a]carbazoles of potential pharmaceutical interest. From biogenetic point of view, there exists a possibility for the formation of these compounds in the plant body; yet their isolation has not been reported. Hence, it needs further extensive search in plant material for their presence.

3.4. Conclusion

In our attempt directed towards the synthesis of aminocarbazole derivatives, via 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles and 1-semicolonazono-1,2,3,4-tetrahydrocarbazoles resulted in the formation of 1,N,N-diacetylaminocarbazole derivatives. A plausible mechanism for the formation of products has been proposed.

2-Thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles obtained from the condensation of 1-oxo-1,2,3,4-tetrahydrocarbazoles and thiophene-2-carbaldehyde were successfully irradiated with UV light to 2-thienyl-3,4-dihydrooxeteno[2,3-a]carbazoles.

2-Benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles obtained from the condensation of 1-oxo-1,2,3,4-tetrahydrocarbazoles and benzaldehyde were used as synthons to derive novel 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]- and 4-phenyl-1H-3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]-carbazoles in quantitative yield.

Acylation of 1-hydroxycarbazoles with 3,3-dimethylacryloyl chloride in presence of aluminium iodide in acetonitrile yielded a mixture of three products, 2-(3',3'-dimethylacryloyl)-1-hydroxycarbazoles, 2,2,-dimethyl-6-(3',3'-dimethylacryloyl)-2H-11H-indolo[3,2-h]chroman-4-ones and 2,2-dimethyl-2H-11H-indolo[3,2-h]chroman-4-ones. Biogenetically possible and hitherto unknown carbazole derivatives, 4-oxo-2-phenylpyrano[2,3-a]carbazoles from 1-hydroxycarbazoles via 1-hydroxy-2-cinnamoylcarbazoles and 2-methyl-4-oxopyrano[2,3-a]carbazoles directly from 1-
hydroxycarbazoles and ethyl acetate in presence of zinc chloride and phosphorus oxychloride or polyphosphoric acid were successfully prepared for the first time.

Experimental

Starting materials:

Synthesis of 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles (2a-e) from 1-oxo-1,2,3,4-tetrahydrocarbazoles (1a-e)

General procedure: The respective 1-oxo-1,2,3,4-tetrahydrocarbazole (1, 0.005 mol), thiosemicarbazide hydrochloride (0.01 mol) and sodium acetate (0.01 mol) in 6 mL water were refluxed in ethanol (30 mL) for 10 h. The solid that separated out from the solution on cooling was filtered and recrystallized from ethanol.

1-Thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a)

1-Oxo-1,2,3,4-tetrahydrocarbazole (1a) : 0.925 g (0.005 mol)
Yield : 1.161 g (90%)
Mp : 213°C
IR (KBr) [v max cm⁻¹] (Fig 1) : 3440, 3300, 3145, 2922, 1577, 1515, 1498, 1325, 1244, 746
¹H NMR (CDCl₃) [δ ppm] (Fig 2) : 1.93-1.96 (p, 2H, C₃-H₂), 2.69-2.73 (m, 2H, C₂-H₂), 2.75-2.78 (m, 2H, C₄-H₂), 7.49 (d, 1H, C₅-H, J=8.00 Hz), 7.32 (d, 1H, C₈-H, J=8.00 Hz), 7.16 (t, 1H, C₇-H, J=7.58 Hz), 6.99 (t, 1H, C₆-H, J=7.58 Hz), 8.29 (s, 2H, NH₂), 10.47 (s, 1H, indole NH), 11.20 (s, 1H, NHCS)
Analysis (C₁₃H₁₄N₄S) Calcd : C, 60.44; H, 05.46; N, 21.69%
Found : C, 60.53; H, 05.29; N, 21.68%

6-Methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2b)

6-Methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1b) : 0.995 g (0.005 mol)
Yield : 1.251 g (92%)
Mp : 222°C
IR (KBr) [v max cm⁻¹] : 3440, 3289, 3146, 1582, 1524, 1496, 1322, 1243, 743
¹H NMR (CDCl₃) [δ ppm] : 1.92-1.97 (m, 2H, C₃-H₂), 2.40 (s, 3H, C₆-CH₃), 2.60-3.12 (m, 4H, C₂-H₂, C₄-H₂), 6.92-7.32 (m, 3H, C₅-H, C₇-H, C₈-H), 8.25 (s, 2H, NH₂), 10.50 (s, 1H, indole NH), 11.12 (s, 1H,
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Analysis (C₁₄H₁₆N₄S) Calcd
Found

NHC₅)
C, 61.74; H, 05.92; N, 20.57%
C, 61.78; H, 05.82; N, 20.62%

7-Methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2c)

7-Methyl-1-oxo-1,2,3,4-
tetrahydrocarbazole (1c)
Yield
Mp
IR (KBr) [v max cm⁻¹]
¹H NMR (CDCl₃) [δ ppm]
(Fig 23)
Analysis (C₁₄H₁₆N₄S) Calcd
Found

: 0.995 g (0.005 mol)
: 1.156 g (85%)
: 219°C
: 3441, 3282, 3152, 1585, 1592, 1524, 1463, 1324, 1256, 728
: 1.92-1.98 (m, 2H, C₅-H₂), 2.39 (s, 3H, C₇-CH-0, 2.67-2.75 (m, 4H, C₂-H₂, C₄-H₂), 6.83 (d, 1H, C₅-H, J=8.00 Hz), 7.09 (s, 1H, C₈-H), 7.37 (d, 1H, C₆-H, J=8.00 Hz), 8.27 (s, 2H, NH₂), 10.45 (s, 1H, indole NH), 11.05 (s, 1H, NHCS)
: C, 61.74; H, 05.92; N, 20.57%
: C, 61.80; H, 05.95; N, 20.59%

8-Methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2d)

8-Methyl-1-oxo-1,2,3,4-
tetrahydrocarbazole (1d)
Yield
Mp
IR (KBr) [v max cm⁻¹]
¹H NMR (CDCl₃) [δ ppm]
(Fig 24)
Analysis (C₁₄H₁₆N₄S) Calcd
Found

: 0.995 g (0.005 mol)
: 1.183 g (87%)
: 218°C
: 3450, 3282, 3163, 1592, 1588, 1456, 1320, 1260, 739
: 1.90-1.99 (m, 2H, C₅-H₂), 2.50 (s, 3H, C₇-CH₃), 2.53-2.76 (m, 2H, C₂-H₂), 3.04 - 3.34 (m, 2H, C₄-H₂), 6.90-7.49 (m, 3H, C₅-H, C₆-H, C₇-H), 8.52 (s, 2H, NH₂), 10.40 (s, 1H, indole NH), 11.22 (s, 1H, NHCS)
: C, 61.74; H, 05.92; N, 20.57%
: C, 61.80; H, 05.95; N, 20.59%

6-Chloro-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2e)

6-Chloro-1-oxo-1,2,3,4-
tetrahydrocarbazole (1e)
Yield
Mp
IR (KBr) [v max cm⁻¹]
Analysis (C₁₄H₁₀N₄S) Calcd
Found

: 0.995 g (0.005 mol)
: 1.358 g (93%)
: 243°C
: 3449, 3289, 3169, 1592, 1595, 1453, 1322, 1262, 750
: C, 61.92; H, 05.77; N, 20.45%
Synthesis of 1-N,N-diacetylamino carbazoles (4a-e) from 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazoles (2a-e)

**General procedure:** 1-Thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2, 0.004 mol) was dissolved in 5 mL of acetic anhydride and refluxed for 2 h, cooled, poured into crushed ice and extracted using ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate, filtered and evaporated. The residue was purified by column chromatography using 97:3 petroleum ether-ethyl acetate mixture.

### 1-N,N-Diacetylamino carbazole (4a)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) $[\nu_{\text{max}} \text{ cm}^{-1}]$</th>
<th>$^{1}\text{H NMR (CDCl}_3 \text{) [δ ppm]}$ (Fig 4)</th>
<th>Analysis (C$<em>{16}$H$</em>{14}$N$_2$O$_2$) Calcd</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a)</td>
<td>1.032 g (0.004 mol)</td>
<td>0.712 g (67%)</td>
<td>128 °C</td>
<td>3350, 1680, 1610, 1371, 1268, 948, 785</td>
<td>2.29 &amp; 2.43 (2 s, 6H, N(COCH$_3$)$_2$), 7.01 (t, 1H, C$_6$-H, J=7.92 Hz), 7.21 (t, 1H, C$_7$-H, J=7.92 Hz), 7.30-7.34 (m, 2H, C$_3$-H, C$_5$-H), 7.48 (d, 1H, C$_8$-H, J=8.00 Hz), 7.82 (d, 1H, C$_4$-H, J=8.00 Hz), 7.97 (d, 1H, C$_2$-H, J=8.00 Hz), 8.79 (s, 1H, NH)</td>
<td>C, 72.16; H, 05.30; N, 10.52%</td>
<td>C, 72.25; H, 05.22; N, 10.69%</td>
</tr>
</tbody>
</table>

### 6-Methyl-1-N,N-diacetylamino carbazole (4b)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) $[\nu_{\text{max}} \text{ cm}^{-1}]$</th>
<th>$^{1}\text{H NMR (CDCl}_3 \text{) [δ ppm]}$ (Fig 4)</th>
<th>Analysis (C$<em>{16}$H$</em>{14}$N$_2$O$_2$) Calcd</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-Methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2b)</td>
<td>1.088 g (0.004 mol)</td>
<td>0.722 g (69%)</td>
<td>160 °C</td>
<td>3498, 1672, 1612, 1412, 1382, 1274, 950, 783</td>
<td>2.29 &amp; 2.43 (2 s, 6H, N(COCH$_3$)$_2$), 7.01 (t, 1H, C$_6$-H, J=7.92 Hz), 7.21 (t, 1H, C$_7$-H, J=7.92 Hz), 7.30-7.34 (m, 2H, C$_3$-H, C$_5$-H), 7.48 (d, 1H, C$_8$-H, J=8.00 Hz), 7.82 (d, 1H, C$_4$-H, J=8.00 Hz), 7.97 (d, 1H, C$_2$-H, J=8.00 Hz), 8.79 (s, 1H, NH)</td>
<td>C, 72.16; H, 05.30; N, 10.52%</td>
<td>C, 72.25; H, 05.22; N, 10.69%</td>
</tr>
</tbody>
</table>
Studies in Heterocycles

$^1$H NMR (CDCl$_3$) [δ ppm] (Fig 26)

- 2.38 (s, 3H, C$_6$-CH$_3$), 2.47 (2 s, 6H, N(COCH$_3$)$_2$), 7.09 (t, 1H, C$_7$-H, J=7.92 Hz), 7.22 (d, 1H, C$_7$-H, J=8.00 Hz), 7.39 (d, 1H, C$_8$-H, J=8.00 Hz), 7.44 (d, 1H, C$_4$-H, J=8.00 Hz), 7.69 (s, 1H, C$_5$-H), 8.05 (d, 1H, C$_2$-H, J=8.00 Hz), 10.00 (s, 1H, NH)

Analysis (C$_{17}$H$_{16}$N$_2$O$_2$) Calcd

- C, 72.84; H, 05.75; N, 09.99%

7-Methyl-1-N,N-diacetylamino-carbazole (4c)

- 7-Methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2c)
  - 1.088 g (0.004 mol) Yield: 0.874 g (78%)
  - Mp: 198°C
  - IR (KBr) [v max cm$^{-1}$]: 3474, 1676, 1615, 1414, 1382, 1272, 986, 772
  - $^1$H NMR (CDCl$_3$) [δ ppm] (Fig 27)
    - 7.03 (d, 1H, C$_6$-H, J=8.00 Hz), 7.07 (d, 1H, C$_7$-H, J=3.7 Hz), 7.19 (s, 1H, C$_8$-H), 7.32 (t, 1H, C$_5$-H, J=7.92 Hz), 7.73 (d, 1H, C$_4$-H, J=8.00 Hz), 7.99 (d, 1H, C$_2$-H, J=8.00 Hz)

Analysis (C$_{17}$H$_{16}$N$_2$O$_2$) Calcd

- C, 72.84; H, 05.75; N, 09.99%

8-Methyl-1-N,N-diacetylamino-carbazole (4d)

- 8-Methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2d)
  - 1.088 g (0.004 mol) Yield: 0.728 g (65%)
  - Mp: 110°C
  - IR (KBr) [v max cm$^{-1}$]: 3498, 1670, 1613, 1412, 1380, 1276, 953, 780
  - $^1$H NMR (CDCl$_3$) [δ ppm] (Fig 27)
    - 7.12 (t, 1H, C$_7$-H, J=7.92 Hz), 7.23-7.39 (m, 3H, C$_3$-H, C$_6$-H, C$_7$-H), 7.42 (d, 1H, C$_4$-H, J=8.00 Hz), 8.08 (d, 1H, C$_2$-H, J=8.00 Hz)

Analysis (C$_{17}$H$_{16}$N$_2$O$_2$) Calcd

- C, 72.84; H, 05.75; N, 09.99%

6-Chloro-1-N,N-diacetylamino-carbazole (4e)

- 6-Chloro-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2e)
  - 1.168 g (0.01 mol) Yield: 0.840 g (70%)

Kavitha C, 2002 134
Synthesis of 1-N,N-diacylaminocarbazoles (4a-e) from 1-semicarbazono-1,2,3,4-tetrahydrocarbazoles (3a-e)

**General procedure:** 1-Semicarbazono-1,2,3,4-tetrahydrocarbazole\(^{(3)}\) (3, 0.004 mol) was dissolved in 5 mL of acetic anhydride and refluxed for 2 h, cooled, poured into crushed ice and extracted using ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate, filtered and evaporated. The residue was purified by column chromatography using 97:3 petroleum ether-ethyl acetate mixture.

**1-N,N-Diacetylaminocarbazole (4a)**

1-Semicarbazono-1,2,3,4-tetrahydrocarbazole (3a) Yield: 0.659 g (62%) The product was found to be identical with 1-N,N-Diacetylaminocarbazole (4a) derived from 1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2a) in all respects (mp, mixed mp, co-tlc, superimpossable IR, \(^1\)H NMR).

**6-Methyl-1-N,N-diacylaminocarbazole (4b)**

6-Methyl-1-semicarbazono-1,2,3,4-tetrahydrocarbazole (3b) Yield: 0.728 g (65%) The product was found to be identical with 6-methyl-1-N,N-Diacetylaminocarbazole (4b) derived from 6-methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2b) in all respects (mp, mixed mp, co-tlc, superimpossable IR, \(^1\)H NMR).

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Kavitha C, 2002
7-Methyl-1-N,N-diacetylamino carbazole (4c)
7-Methyl-1-semicarbazono-1,2,3,4-tetrahydrocarbazole (3c) : 1.024 g (0.004 mol)
Yield : 0.818 g (73%)

The product was found to be identical with 7-methyl-1-N,N-Diacetylamino carbazole (4c) derived from 7-methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2c) in all respects (mp, mixed mp, co-tlc, superimpossible IR, $^1$H NMR).

8-Methyl-1-N,N-diacetylamino carbazole (4d)
8-Methyl-1-semicarbazono-1,2,3,4-tetrahydrocarbazole (3d) : 1.024 g (0.004 mol)
Yield : 0.806 g (72%)

The product was found to be identical with 8-methyl-1-N,N-Diacetylamino carbazole (4d) derived from 8-methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2d) in all respects (mp, mixed mp, co-tlc, superimpossible IR, $^1$H NMR).

6-Chloro-1-N,N-diacetylamino carbazole (4e)
6-Chloro-1-semicarbazono-1,2,3,4-tetrahydrocarbazole (3e) : 1.104 g (0.004 mol)
Yield : 0.792 g (66%)

The product was found to be identical with 6-chloro-1-N,N-Diacetylamino carbazole (4e) derived from 6-methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2e) in all respects (mp, mixed mp, co-tlc, superimpossible IR, $^1$H NMR).

Synthesis of 2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (5a-e) from 1-oxo-1,2,3,4-tetrahydrocarbazoles (1a-e)

General procedure: An equimolar mixture of respective 1-oxo-1,2,3,4-tetrahydrocarbazole (1, 0.004 mol) and thiophene-2-carbaldehyde (0.004 mol) was treated with 4 % alc potassium hydroxide solution (15 mL) and the mixture was stirred for 6 h at room temperature. The precipitated product was filtered off and washed with 50% ethanol. A further crop of condensation product was obtained on neutralization with acetic acid and dilution with water. The products were crystallized from methanol.
1-Oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5a)

<table>
<thead>
<tr>
<th>&lt;sup&gt;1&lt;/sup&gt;Oxo-1,2,3,4-tetrahydrocarbazole (1a) &gt; 0.740 g (0.004 mol)</th>
<th>Yield &gt; 0.837 g (75%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mp &gt; 224°C</td>
<td>IR (KBr) [(\nu_{\text{max}}) cm(^{-1})] &gt; 3275, 1635, 1570, 1520, 1465, 1350, 1260</td>
</tr>
<tr>
<td>(Fig 5)</td>
<td>[^1\text{H NMR (CDCl\textsubscript{3}) [(\delta) ppm]}] &gt; 3.02 (m, 2H, C\textsubscript{3}-H\textsubscript{2}), 3.26 (m, 2H, C\textsubscript{4}-H\textsubscript{2}), 3.75-7.63 (m, 7H, aromatic-H), 7.80 (s, 1H, thienylic-H), 9.21 (bs, 1H, NH)</td>
</tr>
<tr>
<td>(Fig 6)</td>
<td>Analysis (C\textsubscript{17}H\textsubscript{13}NOS) Calcd &gt; C, 73.09; H, 04.69; N, 05.01%</td>
</tr>
<tr>
<td>Found &gt; C, 72.93; H, 04.60; N, 04.95%</td>
<td></td>
</tr>
</tbody>
</table>

6-Methyl-1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5b)

6-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1b) &gt; 0.796 g (0.004 mol) | Yield &gt; 0.879 g (75%) |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Mp &gt; 235°C</td>
<td>IR (KBr) [(\nu_{\text{max}}) cm(^{-1})] &gt; 3290, 1630, 1575, 1560, 1475, 1340, 1290</td>
</tr>
<tr>
<td>(Fig 29)</td>
<td>[^1\text{H NMR (CDCl\textsubscript{3}) [(\delta) ppm]}] &gt; 2.45 (s, 3H, C\textsubscript{6}-CH\textsubscript{3}), 3.13 (m, 2H, C\textsubscript{3}-H\textsubscript{2}), 3.35 (m, 2H, C\textsubscript{4}-H\textsubscript{2}), 7.13-7.50 (m, 6H, aromatic-H), 7.96 (s, 1H, thienylic-H), 8.93 (bs, 1H, NH)</td>
</tr>
<tr>
<td>Analysis (C\textsubscript{18}H\textsubscript{15}NOS) Calcd &gt; C, 73.69; H, 05.15; N, 04.77%</td>
<td></td>
</tr>
<tr>
<td>Found &gt; C, 73.74; H, 05.01; N, 04.74%</td>
<td></td>
</tr>
</tbody>
</table>

7-Methyl-1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5c)

7-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1c) &gt; 0.796 g (0.004 mol) | Yield &gt; 0.891 g (76%) |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mp &gt; 258°C</td>
<td>IR (KBr) [(\nu_{\text{max}}) cm(^{-1})] &gt; 3285, 1635, 1590, 1535, 1480, 1345, 1275</td>
</tr>
<tr>
<td>[^1\text{H NMR (CDCl\textsubscript{3}) [(\delta) ppm]}] &gt; 2.53 (s, 3H, C\textsubscript{7}-CH\textsubscript{3}), 3.10 (m, 2H, C\textsubscript{3}-H\textsubscript{2}), 3.31 (m, 2H, C\textsubscript{4}-H\textsubscript{2}), 7.07-7.56 (m, 6H, aromatic-H), 7.89 (s, 1H, thienylic-H), 8.72 (bs, 1H, NH)</td>
<td></td>
</tr>
<tr>
<td>Analysis (C\textsubscript{18}H\textsubscript{15}NOS) Calcd &gt; C, 73.69; H, 05.15; N, 04.77%</td>
<td></td>
</tr>
<tr>
<td>Found &gt; C, 73.71; H, 05.04; N, 04.71%</td>
<td></td>
</tr>
</tbody>
</table>

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8-Methyl-1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5d)

8-Methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1d)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>0.914 g (78%)</td>
</tr>
<tr>
<td>Mp</td>
<td>260°C</td>
</tr>
<tr>
<td>IR (KBr) $[\nu_{\text{max}} \text{ cm}^{-1}]$</td>
<td>3200, 1635, 1580, 1470, 1345, 1270</td>
</tr>
<tr>
<td>$^1$H NMR (CDCl$_3$) $[\delta \text{ ppm}]$</td>
<td>2.53 (s, 3H, C$_8$-CH$_3$), 3.14 (m, 2H, C$_3$-H$_2$), 3.35 (m, 2H, C$_4$-H$_2$), 7.05–7.48 (m, 6H, aromatic-H), 7.92 (s, 1H, thienylic-H), 8.83 (b s, 1H, NH)</td>
</tr>
</tbody>
</table>

Analysis (C$_{18}$H$_{15}$NOS) Calcd: C, 73.69; H, 5.15; N, 4.77%
Found: C, 73.70; H, 5.03; N, 4.70%

6-Chloro-1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5e)

6-chloro-1-oxo-1,2,3,4-tetrahydrocarbazole (1e)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>0.876 g (70%)</td>
</tr>
<tr>
<td>Mp</td>
<td>270°C</td>
</tr>
<tr>
<td>IR (KBr) $[\nu_{\text{max}} \text{ cm}^{-1}]$</td>
<td>3230, 1645, 1540, 1365, 1325, 1270</td>
</tr>
<tr>
<td>$^1$H NMR (CDCl$_3$) $[\delta \text{ ppm}]$</td>
<td>3.12 (m, 2H, C$_3$-H$_2$), 3.36 (m, 2H, C$_4$-H$_2$), 7.14–7.65 (m, 6H, aromatic-H), 7.96 (s, 1H, thienylic-H), 9.02 (b s, 1H, NH)</td>
</tr>
</tbody>
</table>

Analysis (C$_{17}$H$_{12}$NOSCl) Calcd: C, 65.06; H, 3.85; N, 4.46%
Found: C, 65.01; H, 3.76; N, 4.39%

Synthesis of 2-thienyl-3,4-dihydrooxeteno[2,3-a]carbazoles (6a-e) from 2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (5a-e)

General procedure: 2-Thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5, 0.004 mol) in sodium dried benzene (150 mL) was irradiated with UV light of wavelength 253.7 nm for 36 h in a quartz tube. The excess solvent was removed at 50°C using rota evaporator. The resulting residue was purified by column chromatography over silica gel using petroleum ether-ethyl acetate mixture (98:2) and the compounds were crystallized from the same solvent mixture.

2-Thienyl-3,4-dihydrooxeteno[2,3-a]carbazole (6a)

2-Thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5a)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.116 g (0.004 mol)</td>
</tr>
</tbody>
</table>
Studies in Heterocycles

Yield : 0.803 g (72%)
Mp : 245°C
IR (KBr) \( [\nu_{\text{max}} \text{ cm}^{-1}] \)
(Fig 7)
\( ^1\text{H NMR (CDCl}_3\) \( [\delta \text{ ppm}] \)
(Fig 8)
Analysis (C\(_{17}\)H\(_{13}\)NOS) Calcd
Found

3,4-Dihydro-6-methyl-2-thienyloxeteno[2,3-a]carbazole (6b)
6-Methyl-2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5b)
Yield : 0.855 g (73%)
Mp : 240°C
IR (KBr) \( [\nu_{\text{max}} \text{ cm}^{-1}] \)
\( ^1\text{H NMR (CDCl}_3\) \( [\delta \text{ ppm}] \)
Analysis (C\(_{18}\)H\(_{15}\)NOS) Calcd
Found

3,4-Dihydro-7-methyl-2-thienyloxeteno[2,3-a]carbazole (6c)
7-Methyl-2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5c)
Yield : 0.796 g (68%)
Mp : 249°C
IR (KBr) \( [\nu_{\text{max}} \text{ cm}^{-1}] \)
\( ^1\text{H NMR (CDCl}_3\) \( [\delta \text{ ppm}] \)
Analysis (C\(_{18}\)H\(_{15}\)NOS) Calcd
Found

3,4-Dihydro-8-methyl-2-thienyloxeteno[2,3-a]carbazole (6d)
8-Methyl-2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5d)
Yield : 0.773 g (66%)
Mp : 250°C
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3,4-Dihydro-6-chloro-2-thienyloxeteno[2,3-a]carbazole (6e)

6-Chloro-2-thienylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (5e)

Yield: 1.252 g (0.004 mol)
MP: 262°C
IR (KBr) [v max cm⁻¹]: 3250, 1600, 1540, 1410, 1380, 1290, 1210, 989
'H NMR (CDCl₃) [δ ppm]: 2.46 (s, 3H, C₈-CH₃), 3.12-3.40 (m, 4H, C₃-H₂, C₄-H₂), 6.98 (s, 1H, olefinic-H), 7.10-7.59 (m, 6H, aromatic-H), 8.92 (b s, 1H, NH)
Analysis (C₁₈H₁₅NOS) Calcd: C, 73.69; H, 05.15; N, 04.77%
Found: C, 73.70; H, 05.22; N, 04.93%

Synthesis of 2-N-acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazoles (8a-e) from 2-benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (7a-e)

General procedure: 2-Benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazole⁴₈ (7, 0.001 mol) was refluxed with 0.5 mL hydrazine hydrate (0.01 mol) in acetic acid (3 mL) for 8 h, cooled, poured into crushed ice and extracted with chloroform. The combined organic phase was successively washed with water, dried over anhydrous sodium sulphate and concentrated. The residue was purified by column chromatography over silica gel using petroleum ether-ethyl acetate (80:20) as eluant.

2-N-Acetyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazole (8a)

2-Benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (7a)

Yield: 0.273 g (0.001 mol)
MP: 274°C
IR (KBr) [v max cm⁻¹] (Fig 9):
1'H NMR (CDCl₃) [δ ppm] (Fig 10):
2.39 (s, 3H, N-COCH₃), 1.72, 2.05, 2.84, 3.09, 3.36 (5 m, 5H, C₃a-H, C₄-H₂, C₅-H₂), 4.88 (d,
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13 C NMR (CDCl₃)

Analysis (C₂₁H₁₅N₃O) Calcd

Found

2-N-Acetyl-7-methyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazole (8b)

2-Benzylidene-6-methyl-oxo-1,2,3,4-tetrahydrocarbazole (7b)

Yield

Mp

IR (KBr) [v max cm⁻¹]

'H NMR (CDCl₃) [δ ppm]

(Fig 32)

Analysis (C₂₂H₂₁N₃O) Calcd

Found

2-N-Acetyl-8-methyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazole (8c)

2-Benzylidene-7-methyl-oxo-1,2,3,4-tetrahydrocarbazole (7c)

Yield

Mp

IR (KBr) [v max cm⁻¹]

'H NMR (CDCl₃) [δ ppm]

Analysis (C₂₂H₂₁N₃O) Calcd

Found

2-N-Acetyl-9-methyl-3-phenyl-3,3a,4,5-tetrahydropyrazolino[3,4-a]carbazole (8d)

2-Benzylidene-8-methyl-oxo-1,2,3,4-tetrahydrocarbazole (7d)

Yield

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Mp: 212°C
IR (KBr) [ν max cm⁻¹]: 3432, 1666, 1556, 1240, 815

¹H NMR (CDCl₃) [δ ppm]:
- 2.35 (s, 3H, N-COCH₃), 2.62 (s, 3H, C₉-C₇H₃), 2.00, 2.80, 3.21, 3.39 (4 m, 5H, C₃δ-H, C₄-H₂, C₅-H₂), 4.86 (d, 1H, C₃-H, J=10.42 Hz), 7.01-7.77 (m, 8H, C₂o⁻H, C₂₂-H), 8.49 (s, 1H, NH).

Analysis (C₂₂H₂₁N₃O) Calcd: C, 76.89; H, 6.16; N, 12.29%
Found: C, 76.77; H, 06.20; N, 12.52%

2-N-Acetyl-7-chloro-3-phenyl-3a,4,5-tetrahydropyrazolo[3,4-a]carbazole (8e)

2-Benzylidene-6-chloro-1-oxo-1,2,3,4-tetrahydrocarbazole (7e)

Yield: 0.307 g (0.001 mol)
Mp: 237°C
IR (KBr) [ν max cm⁻¹]: 3439, 1652, 1558, 1243, 812
¹H NMR (CDCl₃) [δ ppm]:
- 2.38 (s, 3H, N-COCH₃), 2.03, 2.81, 2.99, 3.34 (4 m, 5H, C₃δ-H, C₄-H₂, C₅-H₂), 4.87 (d, 1H, C₃-H, J=10.42 Hz), 7.05-7.50 (m, 8H, C₂o⁻H, C₂₂-H), 8.60 (s, 1H, NH).

Analysis (C₂₁H₁₈N₃OCl) Calcd: C, 69.28; H, 04.78; N, 11.60%
Found: C, 69.32; H, 04.78; N, 11.59%

Synthesis of 4-phenyl-1H-3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazoles (9a-e) from 2-benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazoles (7a-b)

General procedure: A mixture of 2-benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (7, 0.001 mol) and thiourea (0.001 mol) in alc potash (2 g KOH in 20 mL ethanol) was refluxed for 8 h. The reaction mixture was then cooled and poured into crushed ice. The solid formed was filtered and chromatographed over silica gel and eluted with petroleum ether-ethyl acetate (80:20) mixture.

4-Phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9a)

2-Benzylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (7a)
Yield: 0.273 g (0.001 mol)
Mp: 220°C
IR (KBr) [ν max cm⁻¹]: 3440, 1595, 1490, 1332, 779, 746
(9a)
¹H NMR (CDCl₃) [δ ppm]:
- 2.87 & 2.98 (2 m, 4H, C₅-H₂, C₆-H₂), 4.50 (d,
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(Fig 12) Analysis (C_{20}H_{17}N_{3}S) Calcd

\[ \begin{align*}
1H, C_4-H, J=8.76 \text{ Hz}, & \quad 6.92-7.69 \text{ (m, 9H, C}_{7,10}-H, C_{2,6}-H), \quad 9.00 \text{ (b s, 1H, indole NH)} \\
\end{align*} \]

\[ \begin{align*}
\text{Found} & \quad C, 72.43; H, 05.17; N, 12.73\% \\
\end{align*} \]

8-Methyl-4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9b)

2-Benzylidene-6-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (7b)

\[ \begin{align*}
\text{Yield} & \quad : 0.287 \text{ g (0.001 mol)} \\
\text{Mp} & \quad : 163^\circ C \\
\text{IR (KBr) [v max cm}^{-1}] & \quad : 3435, 1578, 1492, 1336, 780, 752 \\
{^1H NMR (CDCl}_3 [\delta \text{ ppm}] & \quad : 2.40 \text{ (s, 3H, C}_8-\text{CH}_3), 2.89-3.19 \text{ (m, 4H, C}_5-\text{H}_2, C_6-\text{H}_2), 4.49 \text{ (d, 1H, C}_4-\text{H, J=8.72 Hz), 7.09-} \\
& \quad 7.79 \text{ (m, 8H, C}_2-\text{6-H, C}_7-\text{H, C}_9-\text{H, C}_{10}-\text{H), 9.30 \text{ (b s, 1H, indole NH)}} \\
\end{align*} \]

Analysis (C_{21}H_{19}N_{3}S) Calcd

\[ \begin{align*}
\text{Found} & \quad C, 72.97; H, 05.54; N, 12.22\% \\
\end{align*} \]

9-Methyl-4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9c)

2-Benzylidene-7-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (7c)

\[ \begin{align*}
\text{Yield} & \quad : 0.186 \text{ g (54\%)} \\
\text{Mp} & \quad : 159^\circ C \\
\text{IR (KBr) [v max cm}^{-1}] & \quad : 3498, 1596, 1490, 1325, 777, 750 \\
{^1H NMR (CDCl}_3 [\delta \text{ ppm}] & \quad : 2.48 \text{ (s, 3H, C}_9-\text{CH}_3), 2.99-3.17 \text{ (2 m, 4H, C}_5-\text{H}_2, C_6-\text{H}_2), 4.50 \text{ (d, 1H, C}_4-\text{H, J=8.72 Hz), 6.84-} \\
& \quad 7.64 \text{ (m, 8H, C}_2-\text{6-H, C}_7-\text{H, C}_8-\text{H, C}_{10}-\text{H), 8.92 \text{ (b s, 1H, indole NH)}} \\
\end{align*} \]

Analysis (C_{21}H_{19}N_{3}S) Calcd

\[ \begin{align*}
\text{Found} & \quad C, 72.97; H, 05.54; N, 12.22\% \\
\end{align*} \]

10-Methyl-4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9d)

2-Benzylidene-8-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (7d)

\[ \begin{align*}
\text{Yield} & \quad : 0.210 \text{ g (61\%)} \\
\text{Mp} & \quad : 192^\circ C \\
\text{IR (KBr) [v max cm}^{-1}] & \quad : 3388, 1572, 1452, 1322, 769, 750 \\
{^1H NMR (CDCl}_3 [\delta \text{ ppm}] & \quad : 2.47 \text{ (s, 3H, C}_{10}-\text{CH}_3), 2.92-3.20 \text{ (2 m, 4H, C}_5-\text{H}_2, C_6-\text{H}_2), 4.51 \text{ (d, 1H, C}_4-\text{H, J=8.72 Hz), 7.02-} \\
& \quad 7.65 \text{ (m, 8H, C}_2-\text{6-H, C}_7-\text{H, C}_8-\text{H, C}_{9}-\text{H), } \\
\end{align*} \]
8-Chloro-4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9e)

2-Benzylidene-6-chloro-1-oxo-1,2,3,4-tetrahydrocarbazole (7e)

Yield: 0.307 g (0.001 mol)
Mp: 200°C
IR (KBr) [v max cm⁻¹]: 3450, 1588, 1459, 1329, 778, 749
¹H NMR (CDCl₃) [δ ppm]: 2.99-3.22 (2 m, 4H, C₅-H₂, C₆-H₂), 4.55 (d, 1H, C₄-H, J=8.76 Hz), 7.10-7.69 (m, 8H, C₂-H, C₆-H, C₉-H, C₁₀-H), 9.32 (b s, 1H, indole NH)

Analysis (C₂₁H₁₉N₃S) Calcd: C, 72.97; H, 05.54; N, 12.22%
Found: C, 72.99; H, 05.62; N, 12.48%

Reaction of 1-hydroxycarbazoles (10) with 3,3-dimethylacryloyl chloride

General procedure: A solution of anhydrous aluminium iodide (50 mmol) in acetonitrile was prepared by adding acetonitrile (80 mL) to a mixture of aluminium foil (2.70 g) and iodine (20.52 g) and heating on a boiling water bath for about 8 h. 1-Hydroxycarbazole (10, 0.02 mol) and 3,3-dimethylacryloyl chloride (0.02 mol) in acetonitrile was then added to the freshly prepared anhydrous aluminium iodide solution and refluxed for 5 h, poured into ice water, extracted with ethyl acetate and washed with water and sodium thiosulphate solution. The combined organic layers were dried over anhydrous sodium sulphate. Removal of the solvent gave a mixture of three products, which were separated into its components by passing it through a column of silica gel.

The following fractions were collected
(a) Petroleum ether-ethyl acetate (99:1)
(b) Petroleum ether-ethyl acetate (97:3)
(c) Petroleum ether-ethyl acetate (85:15)
The removal of the solvent from the fraction (a) in all the cases gave 2-(3',3'-dimethylacryloyl)-1-hydroxycarbazoles (11)
The removal of the solvent from the fraction (b) afforded 2,2-dimethyl-6-(3',3'-dimethylacryloyl)-2H-11H-indolo[3,2-h]chroman-4-ones (13)
The removal of the solvent from the fraction (c) in all the cases gave 2,2-dimethyl-2H,11H-indolo[3,2-\(h\)]chroman-4-ones (12).

**Reaction of 1-hydroxycarbazole (10a) with 3,3-dimethylacryloylchloride**
1-Hydroxycarbazole (10a) : 3.66 g (0.02 mol)

2-(3',3'-Dimethylacryloyl)-1-hydroxycarbazole (11a)
Yield : 0.505 g (20%)
Mp : 209°C (Lit\(^{251}\) mp 209°C)

2,2-Dimethyl-2H-11H-indolo[3,2-\(h\)]chroman-4-one (12a)
Yield : 0.531 g (21%)
Mp : 200°C (Lit\(^{251}\) mp 200°C)

2,2-Dimethyl-6-(3',3'-dimethylacryloyl)-2H,11H-indolo[3,2-\(h\)]chroman-4-one (13a)
Yield : 1.735 g (25%)
Mp : 130°C
IR (KBr) \( [v_{\text{max}} \text{ cm}^{-1}] \) : 3400, 1635, 1633, 1522, 1240, 779
\(^1\)H NMR (CDCl\(_3\)) [\( \delta \text{ ppm} \)] : 1.49 & 1.51 (2 s, 6H, C\(_2\)-(CH\(_3\))\(_2\)), 2.17 & 2.20 (2 s, 6H, =C(CH\(_3\))\(_2\)), 3.10 (s, 2H, C\(_3\)-H\(_2\)), 6.90 (s, 1H, olefinic proton), 7.30-7.89 (m, 5H, C\(_5\)-H, C\(_7\)-H, C\(_8\)-H, C\(_9\)-H, C\(_10\)-H), 8.52 (b s, 1H, NH)
Analysis (C\(_{22}\)H\(_{21}\)NO\(_3\)) Calcd : C, 76.06; H, 06.09; N, 04.03%
Found : C, 76.16; H, 06.35; N, 04.09%

**Reaction of 6-methyl-1-hydroxycarbazole (10b) with 3,3-dimethylacryloylchloride**
6-Methyl-1-hydroxycarbazole (10b) : 3.940 g (0.02 mol)

2-(3',3'-Dimethylacryloyl)-6-methyl-1-hydroxycarbazole (11b)
Yield : 1.172 g (21%)
Mp : 210°C (Lit\(^{251}\) mp 210-211°C)

2,2,8-Trimethyl-2H-11H-indolo[3,2-\(h\)]chroman-4-one (12b)
Yield : 1.507 g (27%)
Mp : 215-217°C (Lit\(^{251}\) mp 215-217°C)
2,2,8-Trimethyl-6-(3',3'-dimethylacryloyl)-2H,11H-indolo[3,2-h]chroman-4-one (13b)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>2.310 g (32%)</td>
</tr>
<tr>
<td>Mp</td>
<td>128°C</td>
</tr>
<tr>
<td>IR (KBr) (v_{\text{max}} \text{ cm}^{-1})</td>
<td>3401, 1632, 1601, 1531, 1252, 778</td>
</tr>
<tr>
<td>(^1)H NMR (CDCl(_3)) (\delta \text{ ppm})</td>
<td>1.56 &amp; 1.57 (2 s, 6H, C(_2)-(CH(_3))(_2)), 2.07 &amp; 2.25 (2 s, 6H, =C(CH(_3))(_2)), 2.94 (s, 2H, C(_3)-H(_2)), 6.90 (s, 1H, olefinic proton), 7.39 (d, 1H, C(_9)-H, (J=8.2 \text{ Hz})), 7.51 (s, 1H, C(<em>7)-H), 7.57 (d, 1H, C(</em>{10})-H, (J=8.2 \text{ Hz})), 7.85 (s, 1H, C(_8)-H), 8.45 (b s, 1H, NH)</td>
</tr>
<tr>
<td>Analysis (C(<em>{23})H(</em>{23})N(_3)O(_3)) Calcd</td>
<td>C, 76.43; H, 06.41; N, 03.88%</td>
</tr>
<tr>
<td>Found</td>
<td>C, 76.52; H, 06.44; N, 03.95%</td>
</tr>
</tbody>
</table>

Reaction of 7-methyl-1-hydroxycarbazole (10c) with 3,3-dimethylacryloylchloride

7-Methyl-1-hydroxycarbazole (10c) : 3.940 g (0.02 mol)

2-(3',3'-Dimethylacryloyl)-7-methyl-1-hydroxycarbazole (11c)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>1.283 g (23%)</td>
</tr>
<tr>
<td>Mp</td>
<td>216-217°C (Lit(^{251}) mp 216-217°C)</td>
</tr>
</tbody>
</table>

2,2,9-Trimethyl-2H-11H-indolo[3,2-\(h\)]chroman-4-one (12c)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>1.395 g (25%)</td>
</tr>
<tr>
<td>Mp</td>
<td>191°C (Lit(^{251}) mp 189-191°C)</td>
</tr>
</tbody>
</table>

2,2,9-Trimethyl-6-(3',3'-dimethylacryloyl)-2H,11H-indolo[3,2-\(h\)]chroman-4-one (13c)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>2.816 g (39%)</td>
</tr>
<tr>
<td>Mp</td>
<td>152°C</td>
</tr>
<tr>
<td>IR (KBr) (v_{\text{max}} \text{ cm}^{-1})</td>
<td>3412, 1636, 1639, 1532, 1252, 769</td>
</tr>
<tr>
<td>(^1)H NMR (CDCl(_3)) (\delta \text{ ppm})</td>
<td>1.59 &amp; 1.56 (2 s, 6H, C(_2)-(CH(_3))(_2)), 2.12 &amp; 2.15 (2 s, 6H, =C(CH(_3))(_2)), 2.53 (s, 3H, C(_8)-CH(_3)), 2.87 (s, 2H, C(_3)-H(_2)), 6.92 (s, 1H, olefinic proton), 7.32-7.79 (m, 4H, C(_5)-H, C(_7)-H, C(<em>8)-H, C(</em>{10})-H), 8.53 (b s, 1H, NH)</td>
</tr>
<tr>
<td>Analysis (C(<em>{23})H(</em>{23})N(_3)O(_3)) Calcd</td>
<td>C, 76.43; H, 06.41; N, 03.88%</td>
</tr>
<tr>
<td>Found</td>
<td>C, 76.62; H, 06.38; N, 03.76%</td>
</tr>
</tbody>
</table>
Reaction of 8-methyl-1-hydroxycarbazole (10d) with 3,3-dimethylacryloyl chloride

8-Methyl-1-hydroxycarbazole (10d) : 3.940 g (0.02 mol)

2-(3',3'-Dimethylacryloyl)-8-methyl-1-hydroxycarbazole (11d)

Yield : 1.060 g (19%)
Mp : 176-177°C (Lit\textsuperscript{251} mp 176-177°C)

2,2,10-Trimethyl-2H-11H-indolo[3,2-h]chroman-4-one (12d)

Yield : 1.172 g (21%)
Mp : 203°C (Lit\textsuperscript{251} mp 203-204°C)

2,2,10-Trimethyl-2H-6-(3',3'-dimethylacryloyl)-2H,11H-indolo[3,2-h]chroman-4-one (13d)

Yield : 2.527 g (35%)
Mp : 126°C
IR (KBr) [v \text{ max cm}\textsuperscript{-1}] : 3415, 1640, 1638, 1532, 1253, 779
\textsuperscript{1}H NMR (CDCl\textsubscript{3}) [\delta ppm] : 1.52 & 1.54 (2 s, 6H, C\textsubscript{2}-(CH\textsubscript{3})\textsubscript{2}), 2.12 & 2.21 (2 s, 6H, =C(CH\textsubscript{3})\textsubscript{2}), 2.54 (s, 3H, C\textsubscript{10}-CH\textsubscript{3}), 3.12 (s, 2H, C\textsubscript{3}-H\textsubscript{2}), 6.91 (s, 1H, olefinic proton), 7.32 -7.80 (m, 4H, C\textsubscript{5}-H, C\textsubscript{7}-H, C\textsubscript{8}-H, C\textsubscript{9}-H), 8.50 (b s, 1H, NH):

Analysis (C\textsubscript{23}H\textsubscript{23}NO\textsubscript{3}) Calcd : C, 76.43; H, 06.41; N, 03.88%
Found : C, 76.44; H, 06.82; N, 03.97%

Reaction of 1-oxo-1,2,3,4-tetrahydrocarbazoles (1a-e) with cinnamaldehyde (14a-d)

General procedure: A mixture of respective 1-oxo-1,2,3,4-tetrahydrocarbazole (1, 0.004 mol) and cinnamaldehyde (0.004 mol) was treated with 4% aq KOH (15 mL) and the mixture was stirred for 6 h at room temperature. The precipitated crystalline product was filtered off and washed with 50% ethanol. A further crop of condensation product was obtained on neutralization with acetic acid and dilution with water. The products were crystallized from methanol.

2-Cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14a)

1-Oxo-1,2,3,4-tetrahydrocarbazole (1a) : 0.740 g (0.004 mol)
Yield : 1.016 g (85%)
Studies in Heterocycles

Mp : 212°C
IR (KBr) [v max cm⁻¹] : 3290, 1622, 1556, 1534, 1488, 1400, 963, 729
¹H NMR (CDCl₃) [δ ppm] : 3.14 (m, 4H, C₃-H₂ & C₄-H₂), 7.10-7.69 (m, 12H, C₅,₆-H, C₇-₃-H, C₈-₆-H), 9.01 (b s, 1H, NH)
Analysis (C₂₁H₁₇NO) Calcd
   Found
C, 84.25; H, 05.72; N, 04.68%
6-Methyl-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14b)

6-Methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1b)
Yield : 1.114 g (89%)
Mp : 225°C
IR (KBr) [v max cm⁻¹] : 3288, 1625, 1553, 1552, 1487, 1299, 965, 744
¹H NMR (CDCl₃) [δ ppm] : 2.48 (s, 3H, C₆-CH₃), 3.12 (m, 4H, C₃-H₂ & C₄-H₂), 7.08-7.70 (m, 11H, C₅-H, C₇-H, C₈-H, C₉-₆-H and olefinic protons), 9.00 (b s, 1H, NH)
Analysis (C₂₂H₁₉NO) Calcd
   Found
C, 84.31; H, 06.11; N, 04.47%

7-Methyl-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14c)

7-Methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1c)
Yield : 1.226 g (92%)
Mp : 222°C
IR (KBr) [v max cm⁻¹] : 3284, 1630, 1555, 1544, 1487, 1390, 960, 734
¹H NMR (CDCl₃) [δ ppm] : 2.50 (s, 3H, C₇-CH₃), 3.13 (m, 4H, C₃-H₂ & C₄-H₂), 7.08 (d, 1H, olefinic proton, J=15.01 Hz), 7.15 (d, 1H, olefinic proton, J=15.01 Hz), 7.22-7.68 (m, 9H, C₅-H, C₆-H, C₇-H, C₈-H, C₉-₆-H and one olefinic proton), 8.99 (b s, 1H, NH)
Analysis (C₂₂H₁₉NO) Calcd
   Found
C, 84.31; H, 06.11; N, 04.47%

8-Methyl-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14d)

8-Methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (1d)
Yield : 1.133 g (85%)
Studies in Heterocycles

6-Chloro-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14e)

6-Chloro-1-oxo-1,2,3,4-tetrahydrocarbazole (1e)

Yield : 0.876 g (90%)

Mp : 239°C

IR (KBr) [ν max cm⁻¹] : 3226, 1637, 1560, 1541, 1483, 1300, 970, 750

¹H NMR (CDCl₃) [δ ppm] (Fig 16): 3.08 & 3.17 (2 m, 4H, C₃-H₂ & C₄-H₂), 7.03 (d, 1H, olefinic proton, J=15.34 Hz), 7.18 (d, 1H, olefinic proton, J=15.34 Hz), 7.20-7.65 (m, 9H, C₃-H, C₇-H, C₈-H, C₂-6,8-H and one olefinic proton), 8.96 (b s, 1H, NH)

Analysis (C₂₁H₁₆NOCl) Calcd: C, 75.56; H, 04.83; N, 04.19%
Found: C, 75.68; H, 04.72; N, 04.25%

Synthesis of 4-oxo-2-phenylpyrano[2,3-a]carbazoles (16a-b)

General procedure: A mixture of respective 1-hydroxycarbazole (10, 0.005 mol), cinnamic acid (0.005 mol), freshly fused finely powdered zinc chloride (3 g) and phosphorus oxychloride (4 mL) was kept at room temperature for 24 h, with occasional shaking. The reaction mixture was then poured into crushed ice and the precipitate obtained was filtered, washed with water, dried and chromatographed over silica gel and eluted with 98:2 petroleum ether-ethyl acetate to afford a dark brown crystals of 2-cinnamoyl-1-hydroxycarbazole (16).

2-Cinnamoyl-1-hydroxycarbazole (16a)

1-Hydroxycarbazole (10a) : 0.915 g (0.005 mol)
Yield : 0.782 g (50%)
Studies in Heterocycles

Mp : 232°C
IR (KBr) [v max cm⁻¹] : 3412, 3384, 1626, 1592, 1493, 1356, 1072, 759

¹H NMR (CDCl₃) [δ ppm] : 7.27–8.10 (m, 13H, 11 aromatic-H and 2 olefinic-H), 8.60 (b s, 1H, NH), 13.79 (s, 1H, OH)
(Fig 35)

Analysis (C₂₁H₁₅NO₂) Calcd : C, 80.49; H, 04.82; N, 04.47%
Found : C, 80.52; H, 04.73; N, 04.50%

2-Cinnamoyl-6-methyl-1-hydroxycarbazole (16b)

6-Methyl-1-hydroxycarbazole (10b) : 0.985 g (0.005 mol)
Yield : 0.735 g (45%)
Mp : 220°C
IR (KBr) [v max cm⁻¹] : 3420, 3381, 1630, 1595, 1495, 1353, 1073, 759
(Fig 17)
¹H NMR (CDCl₃) [δ ppm] : 2.53 (s, 3H, C₆-CH₃), 7.31–7.98 (m, 12H, 10 aromatic-H and 2 olefinic-H), 8.50 (b s, 1H, NH), 13.79 (s, 1H, OH)
(Fig 18)
Analysis (C₂₂H₁₇NO₂) Calcd : C, 80.72; H, 05.23; N, 04.28%
Found : C, 80.50; H, 05.12; N, 04.51%

2-Cinnamoyl-7-methyl-1-hydroxycarbazole (16c)

7-Methyl-1-hydroxycarbazole (10c) : 0.985 g (0.005 mol)
Yield : 0.768 g (47%)
Mp : 215°C
IR (KBr) [v max cm⁻¹] : 3422, 3381, 1629, 1595, 1492, 1352, 759
(Fig 16)
¹H NMR (CDCl₃) [δ ppm] : 2.54 (s, 3H, C₇-CH₃), 7.03–7.99 (m, 12H, 10 aromatic-H and 2 olefinic-H), 8.67 (b s, 1H, NH), 13.79 (s, 1H, OH)
(Fig 36)
Analysis (C₂₂H₁₇NO₂) Calcd : C, 80.72; H, 05.23; N, 04.28%
Found : C, 80.62; H, 05.77; N, 04.12%

2-Cinnamoyl-8-methyl-1-hydroxycarbazole (16d)

8-Methyl-1-hydroxycarbazole (10d) : 0.985 g (0.005 mol)
Yield : 0.719 g (44%)
Mp : 226°C
IR (KBr) [v max cm⁻¹] : 3424, 3380, 1630, 1597, 1496, 757
¹H NMR (CDCl₃) [δ ppm] : 2.50 (s, 3H, C₈-CH₃), 7.25–7.86 (m, 12H, 10
Studies in Heterocycles

Oxidative cyclisation of 2-cinnamoyl-1-hydroxycarbazoles (16a-d) to 4-oxo2-phenylpyrano[2,3-a] carbazoles (17a-d)

**General procedure:** The respective 2-cinnamoyl-1-hydroxycarbazole (16, 0.002) was suspended in dimethylsulphoxide (2 mL) and a crystal of iodine added to it. The mixture was refluxed for 10 min, cooled and poured into water. The solid obtained was filtered off, washed with aq sodium thiosulphate and recrystallized from methanol.

### 4-Oxo-2-phenyl pyrano[2,3-a]carbazole (17a)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) [(\nu_{\text{max}}) cm(^{-1})]</th>
<th>'H NMR (CDCl(_3)) [(\delta) ppm]</th>
<th>Analysis (C(<em>{22})H(</em>{17})NO(_2)) Calcd</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Cinnamoyl-1-hydroxycarbazole (16a)</td>
<td>0.366 g (0.002 mol)</td>
<td></td>
<td>3379, 1600 (shouldering starts at 1680), 1532, 1450, 1252, 779</td>
<td>7.16 (s, 1H, C(_3)-H), 7.21–8.70 (m, 11H, aromatic-H)</td>
<td>C, 80.01; H, 04.21; N, 04.50%</td>
<td>C, 80.98; H, 04.34; N, 04.42%</td>
</tr>
</tbody>
</table>

### 8-Methyl-4-oxo-2-phenylpyrano[2,3-a]carbazole (17b)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) [(\nu_{\text{max}}) cm(^{-1})]</th>
<th>'H NMR (CDCl(_3)) [(\delta) ppm]</th>
<th>Analysis (C(<em>{22})H(</em>{17})NO(_2)) Calcd</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Cinnamoyl-6-methyl-1-hydroxycarbazole (16b)</td>
<td>0.394 g (0.002 mol)</td>
<td></td>
<td>3454, 1620 (shouldering starts at 1690), 1596, 1449, 1254, 772</td>
<td>2.49 (s, 3H, C(_8)-CH(_3)), 7.11 (s, 1H, C(_3)-H), 7.25–8.36 (m, 10H, aromatic protons), 10.05 (b s, 1H, NH)</td>
<td>C, 81.21; H, 04.65; N, 04.31%</td>
<td>C, 81.11; H, 04.79; N, 04.16%</td>
</tr>
</tbody>
</table>

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9-Methyl-4-oxo-2-phenylpyrano[2,3-«]carbazole (17c)

2-Cinnamoyl-7-methyl-1-hydroxy carbazole (16c)
Yield : 0.240 g (37%)
Mp : 298°C
IR (KBr) [v max cm⁻¹] : 3380, 1601 (shouldering starts at 1694), 1450, 1253, 776
1H NMR (CDCl₃) [δ ppm] (Fig 38) : 2.17 (s, 3H, C₀–CH₃), 7.13 (s, 1H, C₁-H), 7.17–8.51 (m, 10H, aromatic-H), 10.10 (b s, 1H, NH)
Analysis (C₂₂H₁₅NO₂) Calcd: C, 81.21; H, 4.65; N, 4.31% 
Found: C, 81.72; H, 4.52; N, 4.23%

10-Methyl-4-oxo-2-phenylpyrano[2,3-a]carbazole (17d)

2-Cinnamoyl-8-methyl-1-hydroxy carbazole (16d)
Yield : 0.234 g (36%)
Mp : >300°C
IR (KBr) [v max cm⁻¹] : 3379, 1605 (shouldering starts at 1685), 1580, 1450, 1254, 777
1H NMR (CDCl₃) [δ ppm] : 2.22 (s, 3H, C₁₀–CH₃), 7.00 (s, 1H, C₂-H), 7.20–8.52 (m, 10H, aromatic-H), 10.11 (b s, 1H, NH)
Analysis (C₂₂H₁₅NO₂) Calcd: C, 81.21; H, 4.65; N, 4.31% 
Found: C, 81.22; H, 4.54; N, 4.21%

Synthesis of 2-methyl-4-oxopyrano[2,3-a]carbazoles (20)

General procedure: A mixture of 1-hydroxycarbazole (10, 0.005 mol), ethyl acetoacetate (0.005 mol), freshly fused finely powdered zinc chloride (3 g) and phosphorus oxy chloride (4 mL) was kept at room temperature for 24 h with occasional stirring. The reaction mixture was then poured into crushed ice and the solid separated was filtered washed, dried and chromatographed over silica gel using (97:3) petroleum ether-ethyl acetate mixture to afford 2-methyl-4-oxopyrano[2,3-a]carbazole (20).

A mixture of 1-hydroxycarbazole (10, 0.005 mol) and ethyl acetoacetate (0.005 mol) polyphosphoric acid was heated on a water bath for 7 h and poured into crushed ice. The solid separated was extracted using ethyl acetate washed with water, dried over anhydrous sodium sulphate, filtered and distilled of the excess solvent. The residue thus
obtained was chromatographed over silica gel using (97:3) petroleum ether-ethyl acetate mixture to obtain 2-methyl-4-oxopyran[2,3-\(\alpha\)]carbazole (20) as yellow crystals.

### 2-Methyl-4-oxopyran[2,3-\(\alpha\)]carbazole (20a)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) [(\nu_{max} \text{ cm}^{-1})]</th>
<th>(\text{\textsuperscript{1}}H) NMR (CDCl(_3)) [(\delta) ppm]</th>
<th>Analysis (C(<em>{16})H(</em>{11})NO(_2))</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Hydroxycarbazole (10a)</td>
<td>0.915 g (0.005 mol)</td>
<td>260°C</td>
<td>: 3398, 1650, 1592, 1495, 1260, 820, 791</td>
<td>: 2.56 (s, 3H, C(_2)-CH(_3)), 6.33 (s, 1H, C(_3)-H), 7.31 (t, 1H, C(_8)-H, J=7.28 Hz), 7.43 (d, 1H, C(_6)-H, J=8.24 Hz), 7.46-7.56 (m, 2H, C(<em>9)-H &amp; C(</em>{10})-H), 7.95 (d, 1H, C(_5)-H, J=8.24 Hz), 8.11 (d, 1H, C(_7)-H, J=7.8 Hz), 8.78 (b s, 1H, NH)</td>
<td>: C, 77.09; H, 04.45; N, 05.62%</td>
<td>: C, 77.20; H, 04.54; N, 05.73%</td>
</tr>
<tr>
<td></td>
<td>0.647 g (52%) (ZnCl(_2)/POCl(_3))</td>
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<tr>
<td></td>
<td>0.746 g (60%) (PPA)</td>
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</tr>
</tbody>
</table>

### 2,8-Dimethyl-4-oxopyran[2,3-\(\alpha\)]carbazole (20b)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) [(\nu_{max} \text{ cm}^{-1})]</th>
<th>(\text{\textsuperscript{1}}H) NMR (CDCl(_3)) [(\delta) ppm]</th>
<th>Analysis (C(<em>{17})H(</em>{13})NO(_2))</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-Methyl-1-hydroxycarbazole (10b)</td>
<td>0.985 g (0.005 mol)</td>
<td>220°C</td>
<td>: 3412, 1646, 1595, 1497, 1258, 850, 790</td>
<td>: 2.53 &amp; 2.54 (2 s, 6H, C(_2)-CH(_3) &amp; C(_8)-CH(_3)), 6.58 (s, 1H, C(_3)-H), 6.98 (d, 1H, C(_9)-H, J=8.00 Hz), 7.24 - 7.28 (m, 2H, C(<em>6)-H &amp; C(</em>{10})-H), 7.34 (d, 1H, C(_5)-H J=8.00 Hz), 7.49 (s, 1H, C(_7)-H), 7.83 (s, 1H, NH)</td>
<td>: C, 77.55; H, 04.97; N, 05.32%</td>
<td>: C, 77.37; H, 04.77; N, 05.28%</td>
</tr>
<tr>
<td></td>
<td>0.591 g (45%) (ZnCl(_2)/POCl(_3))</td>
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<tr>
<td></td>
<td>0.669 g (51%) (PPA)</td>
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</tr>
</tbody>
</table>

### 2,9-Dimethyl-4-oxopyran[2,3-\(\alpha\)]carbazole (20c)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>Mp</th>
<th>IR (KBr) [(\nu_{max} \text{ cm}^{-1})]</th>
<th>(\text{\textsuperscript{1}}H) NMR (CDCl(_3)) [(\delta) ppm]</th>
<th>Analysis (C(<em>{17})H(</em>{13})NO(_2))</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-Methyl-1-hydroxycarbazole (10c)</td>
<td>0.985 g (0.005 mol)</td>
<td>223°C</td>
<td>: 3410, 1652, 1593, 1482, 1257, 795</td>
<td>: 2.49 &amp; 2.73 (2 s, 6H, C(_2)-CH(_3) &amp; C(_9)-CH(_3)), 6.49 (s, 1H, C(_3)-H), 6.95 (d, 1H, C(_8)-H, J=8.20 Hz),</td>
<td>: C, 77.09; H, 04.45; N, 05.62%</td>
<td>: C, 77.20; H, 04.54; N, 05.73%</td>
</tr>
<tr>
<td></td>
<td>0.828 g (63%) (ZnCl(_2)/POCl(_3))</td>
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</tr>
<tr>
<td></td>
<td>0.775 g (59%) (PPA)</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

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8-Methyl-1-hydroxycarbazole (10d) : 0.985 g (0.005 mol)
Yield : 0.789 g (60%) (ZnCl\textsubscript{2}/POCl\textsubscript{3})
: 0.828 g (63%) (PPA)
Mp : 211°C
IR (KBr) [\nu_{max} \text{ cm}^{-1}] : 3403, 1648, 1590, 1486, 1258, 780, 734
\textsuperscript{1}H NMR (CDCl\textsubscript{3}) [\delta \text{ ppm}] : 2.60 & 2.61 (2 s, 6H, C\textsubscript{2}-CH\textsubscript{3} & C\textsubscript{10}-CH\textsubscript{3}), 6.65 (s, 1H, C\textsubscript{3}-H), 7.04 - 7.56 (m, 5H, C\textsubscript{6}-H, C\textsubscript{7}-H, C\textsubscript{8}-H & C\textsubscript{9}-H), 7.82 (s, 1H, NH)
Analysis (C\textsubscript{17}H\textsubscript{13}NO\textsubscript{2}) Calcd
: C, 77.55; H, 04.97; N, 05.32%
: C, 77.77; H, 04.90; N, 05.33%

2,10-Dimethyl-4-oxopyrano[2,3-a]carbazole (20d)
Fig 23. $^1$H NMR spectrum of 7-methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2c)

Fig 24. $^1$H NMR spectrum of 8-methyl-1-thiosemicarbazono-1,2,3,4-tetrahydrocarbazole (2d)
Fig 25. $^1$H NMR spectrum of 6-chloro-1-thiosemicarbazone-1,2,3,4-tetrahydrocarbazole (2e)

Fig 26. $^1$H NMR spectrum of 6-methyl-1-N,N-diacylaminocarbazole (4b)
Fig 27. $^1$H NMR spectrum of 7-methyl-1,N,N-diacetylaminocarbazole (4c)

Fig 28. $^1$H NMR spectrum of 6-chloro-1,N,N-diacetylaminocarbazole (4c)
Fig 29. $^1$H NMR spectrum of 6-methyl-1-oxo-2-thienyldene-1,2,3,4-tetrahydrocarbazole (5b)

Fig 30. $^1$H NMR spectrum of 8-methyl-1-oxo-2-thienyldene-1,2,3,4-tetrahydrocarbazole (5d)
Fig 31. $^1$H NMR spectrum of 6-chloro-1-oxo-2-thienylidene-1,2,3,4-tetrahydrocarbazole (5e)

Fig 32. $^1$H NMR spectrum of 2-N-acetyl-7-methyl-3-phenyl-3,3a,4,5-tetrahydropyrazolo[3,4-α]carbazole (8h)
Fig 33. $^1$H NMR spectrum of 9-methyl-4-phenyl-1H,3,4,5,6-tetrahydro-2-thiopyrimido[4,5-a]carbazole (9c)

Fig 34. $^1$H NMR spectrum of 8-methyl-2-cinnamylidene-1-oxo-1,2,3,4-tetrahydrocarbazole (14d)
Fig 35. $^1$H NMR spectrum of 2-cinnamoyl-1-hydroxycarbazole (16a)

Fig 36. $^1$H NMR spectrum of 2-cinnamoyl-7-methyl-1-hydroxycarbazole (16c)
Fig 37. $^1$H NMR spectrum of 4-oxo-2-phenyl pyra[a,2.3-$a$]carbazole (17a)

Fig 38. $^1$H NMR spectrum of 9-methyl-4-oxo-2-phenylpyrano[2.3-$a$]carbazole (17c)
Fig 39. $^1$H NMR spectrum of 2-methyl-4-oxopyrano[2,3-$\alpha$]carbazole (21a)

Fig 40. $^1$H NMR spectrum of 2,9-dimethyl-4-oxopyrano[2,3-$\alpha$]carbazole (20c)