Syntheses of pyrazolo-, isoxazolo-, pyrido- and pyrimido-carbazoles from 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones

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Mixed aldol condensation of 2,3,4,9-tetrahydrocarbazol-1-ones with 3,4-dimethoxybenzaldehyde (veratraldehyde) yielded 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones. These enones on reaction with hydrazine hydrate, hydroxylamine hydrochloride, malononitrile and guanidinium nitrate under different conditions yielded the corresponding pyrazolo[3,4-*a*]-, isoxazolo[3,4-*a*]-, pyrido[2,3-*a*]-, and pyrimido[4,5-*a*]-carbazoles respectively. The molecular and crystal structure of 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydro-1*H*-carbazol-1-one resolved by single crystal X-ray diffraction is discussed.

Keywords: aldol condensation, 3,4-dimethoxybenzaldehyde, fused pyrazoles, isoxazoles, pyridines, pyrimidines, carbazoles, crystal structures

Carbazoles, and in particular carbazole alkaloids, have attracted much interest as synthetic targets since many of their derivatives exhibit a wide range of biological activity.[1-3] These components are considered to represent potential therapeutic agents against a variety of diseases initiated by oxygen-derived free radicals like myocardial and cerebral ischema, arteriosclerosis, inflammation, rheumatism, senility, cancer and autoimmune diseases.[4-10]

Although a large number of reports are available in the literature describing the synthetic methods directed towards ellipticine, olivacine and related tetracyclic compounds,[11-14] the replacement of the pyridine ring in the natural structure by other heteroaromatic systems has been only scantly reported. Pyridocarbazole derivatives have been reported to exhibit anti-cancer and anti-HIV activities,[15-17] and replacement of pyridine in the pyridocarbazole by other heterocyclic rings may lead to interesting variations in the biological activities.[18-20] Hence, we aimed to devise a concise route for synthesising pyrazolo-, isoxazolo-, pyrido-, and pyrimido-carbazole derivatives and searched for suitable synthons to derive these types of carbazole derivatives. From our laboratory, we have reported the synthesis of 2-benzylidene-2,3,4,9-tetrahydrocarbazoles from precursors of the 2,3,4,9-tetrahydrocarbazol-1-one type and these synthons were utilised to prepare many heteroannelated carbazoles.[21-24] In continuation of this work, we here report the use of 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones (**2a**–**e**) as effective synthons for the synthesis of pyrazolo-, isoxazolo-, pyrido- and pyrimido-carbazoles.

Results and discussion

The preparation of the first class of synthons, 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones (**2**), here given for compound **2a**, is as follows: an equimolar mixture of 6-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**1a**) and 3,4-dimethoxybenzaldehyde (veratraldehyde) is stirred in 5% ethanolic potassium hydroxide for 24 h to yield 6-methyl-2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one **2a** as a yellow solid melting at 110–112 °C in 90% yield. The generality of this reaction was tested with other substituted derivatives (**1b–e**) to yield **2b–e** (Scheme 1). All synthons were unambiguously identified by IR and ^{1}H NMR spectroscopy and mass spectrometry. Representative data for 6-methyl-2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2a**) are given below. Synthetic and spectroscopic details for the compounds (**2b–e**) are presented in the Experimental section. For compound **2d** the crystal structure was determined by X-ray diffraction and this is discussed below.

The IR spectrum of compound **2a** shows stretching vibrations at 3252 cm^{-1} and 1640 cm^{-1} due to the presence of NH and C=O groups, respectively. The ^{1}H NMR spectrum exhibits a broad singlet at δ 8.97 due to the presence of the indole NH moiety. Two singlets at δ 7.75 and δ 7.43 account for the C_2–H and C_2'–H atoms, respectively. A pair of doublets at δ 7.34 and 7.21 with J = 8.04 Hz corresponds to the C_5'–H and C_6'–H units, and the presence of C_7–H and C_8–H is indicated by two doublets in the region of δ 7.04 and δ 6.92 with J = 8.26 Hz. A singlet at δ 6.99 is due to C_5–H. Two singlets at δ 3.93 and δ 3.85 account for the C_3'–OCH_3 and C_4'–OCH_3 groups and a multiplet between δ 3.29 and 3.07 corresponds to the C_3 and C_4 protons. A singlet at δ 2.45 indicates the presence of the methyl proton at C_6. In the mass spectrum, the molecular ion peak appears at *m/z* 347.

Single crystals of 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydro-1*H*-carbazol-1-one (**2d**) were grown from ethanol, crystallising in the space group P-1 with two crystallographically independent molecules per unit cell (Fig. 1). The molecules consists of each two mostly planar sp^2 hybridized sections made up by the aromatic indole and veratrole units with rms deviations from planarity of 0.0321 and 0.0373 Å^2 for the indole and 0.0151 and 0.0072 Å^2 for the veratrole moieties. The planarity as a whole is interrupted by two groups in the centre of the molecules, each an sp^3 hybridised ethylene group, which deviates from the mean plane of the indole unit by up to 0.864(2) Å for C9 (0.870(2) Å for C30 in the second molecule), and by a torsional twist between the veratrole and the adjacent C=C double bond of 34.8(1) and 38.4(1)° in both independent molecules, respectively. The twist angles for the molecules as a whole, defined by the dihedral angle between the planes of the indole and veratrole units in both molecules, are 55.64(3) and 48.17(3)°, respectively. Crystallographic details are given in Table 1. Packing in the structure of **2d** is facilitated by a mixture of hydrogen bonding, and π–π and C–H···π contacts, as indicated in Table 2. CCDC 686840 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request.cif.

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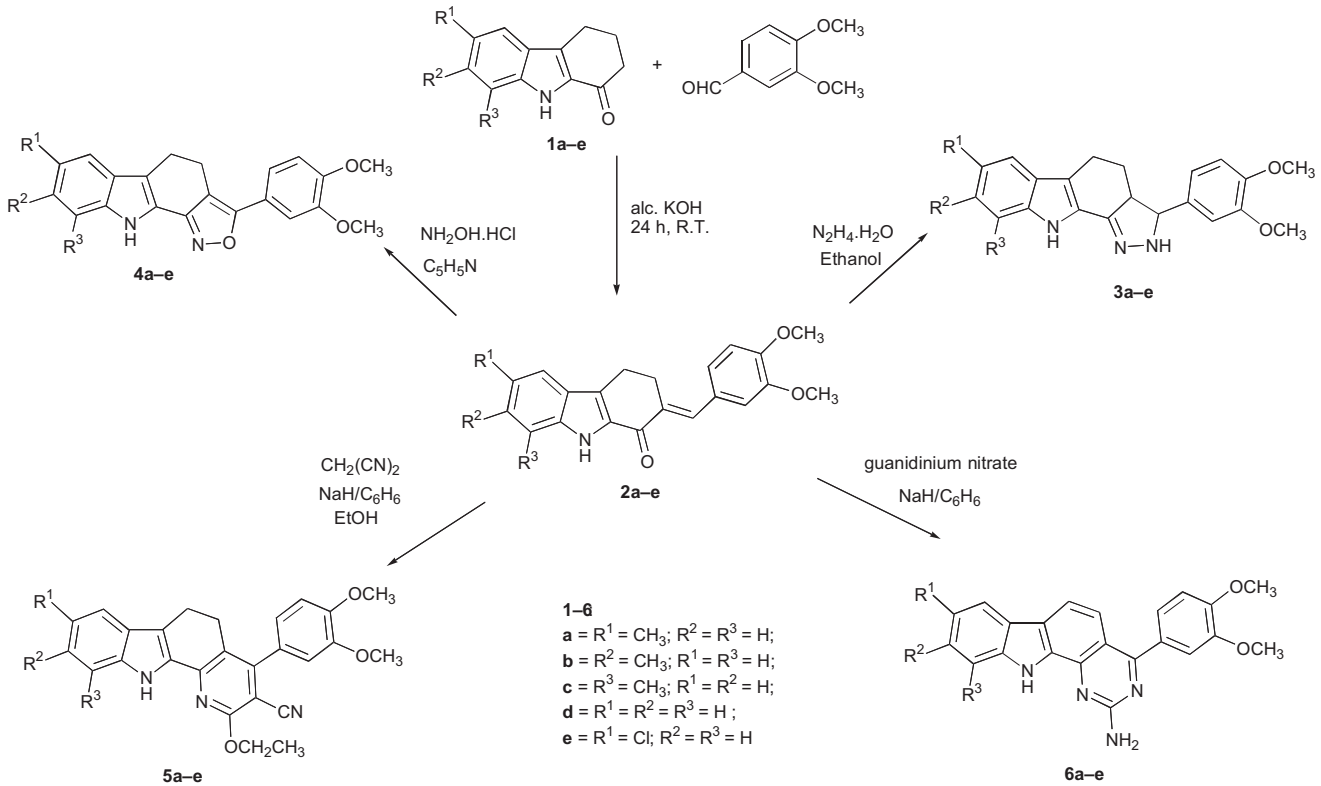


Scheme 1

Table 1 Crystal data for 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2d**)

Chemical formula	$C_{21}H_{19}NO_3$
M_r	333.37
Cell setting, space group	Triclinic, *P*-1
Temperature (K)	100(2)
a, *b*, *c* (Å)	8.779(2), 10.947(3), 18.846(5)
α, β, γ (°)	81.441(4), 86.655(4), 68.210(3)
V (Å^3)	1662.9 (7)
Z	4
D_x (Mg m^{-3})	1.332
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.09
Crystal form, colour	Plate, yellow
Crystal size (mm)	0.61 × 0.40 × 0.09
Absorption correction	Multi-scan
T_{min} and T_{max}	0.847 and 1.000
No. of measured reflections	16824
No. of independent reflections	8142
No. of observed reflections	6915
Criterion for observed reflections	$I > 2\sigma(I)$
R_{int}	0.019
θ_{max} (°)	28.3
Refinement on	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.044, 0.113, 1.02
No. of relections, restraints, parameters	8142, 0, 455
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.37, –0.21

Having obtained the key intermediates, 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones (**2a–e**), our aim was to devise a synthetic route towards the title compounds. Compounds (**2a–e**) were treated with hydrazine hydrate, hydroxylamine hydrochloride, malononitrile and guanidine nitrate, yielding the corresponding pyrazolo[3,4-*a*]- (**3a–e**), isoxazolo[3,4-*a*]- (**4a–e**), pyrido[2,3-*a*]- (**5a–e**), and pyrimido[4,5-*a*]- (**6a–e**) carbazoles respectively (Scheme 1). All the products were examined using IR and ^{1}H NMR spectroscopy and mass spectrometry. Again synthetic and spectroscopic details are given here for the compounds of the

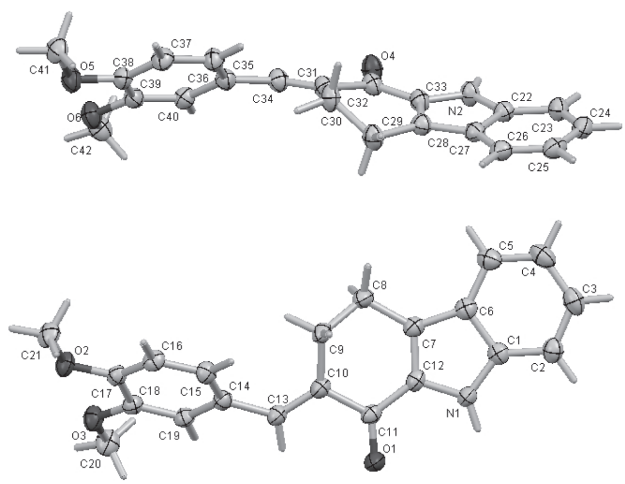


Fig. 1 Thermal ellipsoid representation of both independent molecules of compound **2d** with the atom labelling scheme. Thermal ellipsoids are at the 50% probability level.

a series (compounds **3a**, **4a**, **5a** and **6a** derived from synthon **2a**); details for the compounds of the **b**, **c**, **d** and **e** series are given in the Experimental section.

When **2a** was treated with hydrazine hydrate in ethanol, it afforded the expected 3-(3',4'-dimethoxyphenyl)-2,3,3a,4,5,10-hexahydro-7-methylpyrazolo[3,4-*a*]carbazole (**3a**) – a fused pyrazoline – in 75% yield. Its IR spectrum revealed a band at 1596 cm^{-1} (C=N) and the absence of a carbonyl moiety. The proton NMR spectrum showed a broad singlet at δ 8.60 for the indole NH, and peaks between δ 7.31 and 6.59 for six aromatic protons. The pyrazoline NH proton showed as a broad singlet at δ 5.66. The methoxy groups appeared as singlets at δ 3.97 and 3.95. Multiplets were observed at δ 3.10, δ 2.89, δ 2.78 and δ 2.52 arising from the C_3, C_5, C_{3a} and C_4 protons, respectively, and a singlet at 2.47

Table 2 Hydrogen-bonding interactions, C-H···π and π-π contacts (Å, °) of 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydro-carbazol-1-one (**2d**)

D–H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2–H2A···O4i	0.88	2.10	2.8626 (15)	145
N1–H1···O1i	0.88	2.01	2.8356 (15)	156
C13–H13···O1	0.95	2.40	2.797(2)	104
C34–H34···O2	0.95	2.41	2.7917(19)	104
C4–H4···Cg1iii	0.95	3.2978	3.5399(19)	96.90
C5–H5···Cg3iii	0.95	3.2905	3.3138(18)	83.12
C21–H21···Cg8iv	0.98	3.0410	3.886(2)	145.22
C25–H25···Cg3iii	0.95	2.8661	3.578(2)	132.65
C26–H26···Cg1iii	0.95	3.0453	3.8954(19)	149.67
C42–H42A···Cg5v	0.98	2.7645	3.7194(19)	164.70
C42–H42B···Cg2vi	0.98	3.0470	3.4928(19)	109.10
C42–H42B···Cg6vi	0.98	3.3476	4.166(2)	142.23
C42–H42C···Cg2vi	0.98	3.1198	3.4928(19)	104.27
π–π contacts				
Cg3···Cg3iii	3.8243(14)		Cg8···Cg8vii	3.6452(12)

Symmetry codes: (i) $-x+1, -y, -z+1$; (ii) $-x+2, -y+1, -z+2$; (iii) $1-X,1-Y,1-Z$; (iv) $1+X,-1+Y,-1+Z$; (v) $1+X,-1+Y,-1+Z$; (vi) $1-X,2-Y,2-Z$; (vii) $-X,2-Y,2-Z$

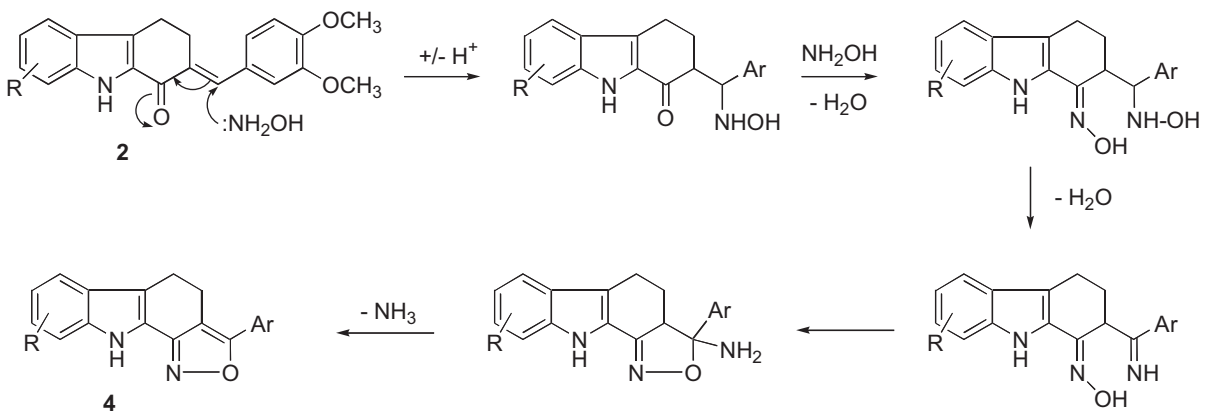
Ring centroids: Cg1 N1 C1 C6 7 C12; Cg2 N2 C22 C27 C28 C33; Cg3 C1 C2 C3 C4 C5 C6; Cg4 C7 C8 C9 C10 C11 C12; Cg5 C14 C15 C16 C17 C18 C19; Cg6 C22 C23 C24 C25 C26 C27; Cg7 C28 C29 C30 C31 C32 C33; Cg8 C35 C36 C37 C38 C39 C40

was due to C_7–CH_3. The mass spectrum and elemental analysis of **3a** lent further support to the assigned structure. Extension of the above reaction under similar conditions to **2b–e** yielded the corresponding carbazole derivatives **3b–e**.

Treatment of 2-(3',4'-dimethoxybenzylidene)-6-methyl-2,3,4,9-tetrahydrocarbazol-1-one (**2a**) with hydroxylamine hydrochloride in dry pyridine yielded a product which was purified by column chromatography. The IR spectrum showed two absorptions at 3436 and 1611 cm^{-1}, ascribable to NH and C=N stretching vibrations respectively. The ^1H NMR spectrum registered a broad singlet at δ 9.05 that showed the presence of an NH proton. A cluster of aromatic peaks between δ 7.52 and 6.80 accounted for six aromatic protons. The appearance of methylene protons as multiplets and methoxy and methyl protons as three singlets were observed in the proton NMR. The molecular ion peak in the mass spectrum appeared at *m/z* 360 and the elemental analysis agreed well with the molecular formula $C_{22}H_{20}N_2O_3$. Based on these data the structure of the product was assigned as 4,5-dihydro-7-methyl-3-(3',4'-dimethoxyphenyl)isoxazolo[3,4-*a*]carbazole (**4a**). The other carbazole derivatives **2b–e** were reacted similarly to yield the corresponding isoxazoles **4b–e**.

A plausible mechanism follows the route of Scheme 2. Hydroxylamine liberated *in situ* from hydroxylamine hydrochloride in the presence of pyridine undergoes 1,4 Michael-type addition to **2** which is followed by further condensation with more hydroxylamine; loss of water molecule from the alkylhydroxylamine group, then cyclisation and finally deamination, gives the final product **4**. Aerial oxidation of an isoxazoline intermediate can be ruled out since **2** yielded **4** also under nitrogen atmosphere.

In consideration of their pharmacological activity[27] it was felt worthwhile to devise a simple route for the synthesis of pyridocarbazoles. Therefore, 2-(3',4'-dimethoxybenzylidene)-6-methyl-2,3,4,9-tetrahydrocarbazol-1-one (**2a**) was dissolved in dry ethanol and reacted with malononitrile in the presence of sodium hydride in dry benzene to give a single product. It showed IR absorption bands at 3330 and 1595 cm^{-1} corresponding to NH and C=N stretching vibrations, and a sharp band at 2214 cm^{-1} indicating the presence of a cyano group. The ^1H NMR spectrum showed a broad singlet at δ 8.75 from the indole NH. Six aromatic protons appeared as doublets and singlets in between the region δ 7.44–6.87. The methylene protons of the ethoxy group at C_2 appear as a quartet at δ 4.64 with J = 7.04 Hz and this downfield shift was attributed to the presence of the cyano group *ortho* to the ethoxy group. Methoxy and methyl protons gave singlets and further methylene protons appeared as multiplets in their corresponding regions; a triplet at δ 1.52 revealed the methyl of the 2-OEt group. The elemental analysis and the molecular ion peak at *m/z* 439 (100%) agreed well with the molecular formula, $C_{27}H_{25}N_3O_3$. Based on the spectral data and elemental analysis, the product was identified as 2-ethoxy-5,6-dihydro-4-(3',4'-dimethoxyphenyl)-8-methyl-pyrido[2,3-*a*]carbazole-3-carbonitrile (**5a**).The reaction was found to be applicable to the other derivatives **2b–e**, forming the corresponding pyridocarbazole-carbonitriles **5b–e**.



Scheme 2

Amino derivatives of carbazoles have potential to be significantly active in the treatment of both Alzheimer's disease and cancer.[28] Incorporation of amino of groups into the carbazole systems would enhance the hydrophilicity of the molecules and therefore increase their water solubility.[29] In addition to this, a large number of reports are available in which heterocyclic pyrimidines with an amino group have pharmacological as well as chemotherapeutic properties;[30] we therefore decided to synthesise several new amino substituted pyrimidocarbazoles. To achieve our target we treated the 2-(3',4'-dimethoxybenzylidene)-6-methyl-2,3,4,9-tetrahydrocarbazol-1-one (**2a**) with guanidine nitrate in the presence of sodium hydride/benzene under reflux for about 18 h, to afford 2-amino-4-(3',4'-dimethoxyphenyl)-8-methylpyrimido[4,5-*a*]carbazole (**6a**) in 69% yield after purification through a silica gel column. The IR spectrum showed absorptions at 3443, 3189 and 3157 cm^{-1} which were assigned to N–H and NH_2 groups. The ^1H NMR spectrum showed a broad singlet at δ 9.55 due to the presence of the NH group. The disappearance of the methylene protons in the aliphatic region and the appearance of further peaks in the aromatic region clearly indicated that the system was fully aromatised. From a broad singlet at δ 5.42 we inferred the presence of an amino group in the substrate. Methoxy and methyl protons appeared as singlets in their respective regions. The elemental analysis and mass spectral data were compatible with the molecular formula $C_{23}H_{20}N_4O_2$. A series of similar reactions were carried out with **2b–e** and similar results were obtained. Mechanistically the amino group of the guanidine nitrate reacts with the carbonyl group of the enone to give the Schiff's base which subsequently undergoes intramolecular 1,4-Michael addition followed by aerial oxidation in presence of NaH/benzene to yield the aromatised product **6.** It should be noted that we have carried out a relatively similar type of reaction with CH_3ONa/EtOH and in that case we isolated 5,6-dihydropyrimidines[31] but in the present case we obtained the fully aromatised product.

In conclusion, pyrazolo[3,4-*a*]-, isoxazolo[3,4-*a*], pyrido [2,3-*a*]- and pyrimido[4,5-*a*]- carbazoles were synthesised from the newly developed synthons 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones **2**, thus opening an easy access to fused carbazoles with hoped-for biological and pharmacological activities. Compound **2d** was also analysed by single crystal X-ray diffraction, providing knowledge of the exact geometry of the molecule.

Experimental

Melting points were determined using a Mettler FP 51 apparatus (Mettler Instruments, Switzerland). IR spectra were recorded using KBr pellets on a Shimadzu FTIR-8201PC spectrophotometer (Shimadzu, Japan). NMR spectra were recorded in $CDCl_3$ on a Varian AMX 400 FT-NMR (Varian Australia) using TMS as internal standard. Mass spectra were recorded on a JEOL-D-300 mass spectrometer. Microanalyses were done on a Vario EL III model CHNS analyser (Vario, Germany). The purity of the products was tested by TLC using plates coated with silica gel G using petroleum ether and ethyl acetate (85:15) as eluent.

Preparation of 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones (**2**)*: general procedure*

An equimolar mixture of the respective substituted 2,3,4,9-tetrahydrocarbazol-1-one (**1a–e**, 0.005 mol) and 3,4-dimethoxybenzaldehyde (0.005 mol) was treated with 5% ethanolic potassium hydroxide (25 ml) and stirred for 24 h at room temperature. The product, precipitating as a yellow crystalline mass, was filtered off and washed with 50% ethanol. A further crop was obtained on neutralisation with acetic acid and dilution with water. The product was recrystallised from methanol to yield the 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-ones (**2a–e**).

2-(3',4'-Dimethoxybenzylidene)-2,3,4,9-tetrahydro-6-methylcarbazol-1-one (**2a**): Yellow solid (1.56 g, 90%), m.p. 110–112 °C. IR: ν_{max} 3252, 2923, 2851, 1640, 1584, 1252, 803 cm^{-1}. ^1H NMR: δ 8.97 (b s, 1H, N_9–H), 7.75 (s, 1H, C_2–H), 7.43 (s, 1H, C_2'–H), 7.34 (d, 1H, C_5'–H, J = 8.04 Hz), 7.21 (d, 1H, C_6'–H, J = 8.04 Hz), 7.04 (d, 1H, C_7 –H, J_m = 1.56 Hz, J_o = 8.26 Hz), 6.99 (s,1H, C_5–H), 6.92 (d, 1H, C_8–H, J = 8.26 Hz), 3.93 (s, 3H, C_3'–OCH_3), 3.85 (s, 3H, C_4'–OCH_3), 3.29–3.07 (m, 4H, C_3–H_2, C_4–H_2), 2.45 (s, 3H, C_6–CH_3). MS: *m/z* (%) 347 (M^+, 100), 332 (18), 272 (11), 258 (21), 183 (26), 169 (10), 115 (16), 76 (19). Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03. Found: C, 76.19; H, 6.15; N, 4.12%.

2-(3',4'-Dimethoxybenzylidene)-2,3,4,9-tetrahydro-7-methylcarbazol-1-one (**2b**): Yellow solid (1.49 g, 86%), m.p. 103–105 °C. IR: ν_{max} 3264, 2927, 2855, 1637, 1580, 1254, 802 cm^{-1}. ^1H NMR: δ 8.85 (b s, 1H, N_9–H), 7.74 (s, 1H, C_2–H), 7.53 (d, 1H, C_5'–H, J = 8.16 Hz), 7.21 (s, 1H, C_2'–H), 7.08 (d, 1H, C_5–H, J = 7.64 Hz), 7.01 (d, 1H, C_6–H, J = 7.64 Hz), 6.98 (s, 1H, C_8–H), 6.91(d, 1H, C_6'–H, J = 8.16 Hz), 3.93 (s, 3H, C_3'–OCH_3), 3.85 (s, 3H, C_4'–OCH_3), 3.30–3.08 (m, 4H, C_3–H_2, C_4–H_2), 2.48 (s, 3H, C_7–CH_3). MS: *m/z* (%) 347 (M^+, 100), 332 (20), 269 (16), 212 (19), 195 (16), 183 (22), 169 (11), 115 (20), 76 (10). Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03. Found: C, 76.10; H, 6.05; N, 4.01%.

2-(3',4'-Dimethoxybenzylidene)-2,3,4,9-tetrahydro-8-methylcarbazol-1-one (**2c**): Yellow solid (1.63 g, 94%), m.p. 145–147 °C. IR: ν_{max} 3237, 2924, 2847, 1643, 1583, 1251, 807 cm^{-1}. ^1H NMR: δ 8.94 (b s, 1H, N_9–H), 7.77 (s, 1H, C_2–H), 7.52 (d, 1H, C_5'–H, J = 7.64 Hz), 7.21–7.18 (m, 2H, C_5–H, C_6–H), 7.09 (s, 1H, C_2'–H), 6.96 (d, 1H, C_7–H, J = 8.04 Hz), 6.92 (d, 1H, C_6'–H, J = 7.64 Hz), 3.94 (s, 3H, C_3'–OCH_3), 3.90 (s, 3H, C_4'–OCH_3), 3.32–3.09 (m, 4H, C_3–H_2, C_4–H_2), 2.52 (s, 3H, C_8–CH_3). MS: *m/z* (%) 347 (M^+, 86), 332 (11), 302 (14), 272 (19), 196 (16), 183 (20), 137 (18), 115 (16), 107 (11), 86 (17).Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03. Found: C, 76.21; H, 5.98; N, 4.07%.

2-(3',4'-Dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2d**): Yellow solid (1.53 g, 92%), m.p. 108–111 °C. IR: ν_{max} 3240, 2925, 2843, 1643, 1587, 1258, 1022, 805 cm^{-1}. ^1H NMR: δ 8.87 (b s, 1H, N_9–H), 7.75 (s, 1H, C_2–H), 7.68 (d, 1H, C_5'–H, J = 8.16 Hz), 7.39–7.10 (m, 4H, C_5, C_6, C_7, C_8–H), 6.99 (s, 1H, C_2'–H), 6.92 (d, 1H, C_6'–H, J = 8.16 Hz), 3.95 (s, 3H, C_3'–OCH_3), 3.92 (s, 3H, C_4'–OCH_3), 3.31–3.09 (m, 4H, C_3–H_2, C_4–H_2). MS: *m/z* (%) 333 (M^+, 100), 302 (16), 271 (18), 257 (10), 195 (12), 182 (13), 137 (16), 114 (26), 105 (22), 77 (18). Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.40; H, 5.85; N, 4.09%.

6-Chloro-2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2e**): Yellow solid (1.63 g, 89%), m.p. 117–119 °C. IR: ν_{max} 3252, 2923, 2851, 1640, 1584, 1252, 803 cm^{-1}. ^1H NMR: δ 8.96 (b s, 1H, N_9–H), 7.76 (s, 1H, C_2–H), 7.38 (s, 1H, C_2'–H), 7.64 (d, 1H, C_5'–H, J = 8.32 Hz), 7.34 (d, 1H, C_6'–H, J = 8.32 Hz), 7.10 (d, 1H, C_7 –H, J_m = 1.92 Hz, J_o = 8.16 Hz), 7.01 (s, 1H, C_5–H), 6.94 (d, 1H, C_8–H, J = 8.16 Hz), 3.94 (s, 3H, C_3'–OCH_3), 3.92 (s, 3H, C_4'–OCH_3), 3.30–3.08 (m, 4H, C_3–H_2, C_4–H_2). MS: *m/z* (%) 369/367 (M^+, 31/100), 332 (19), 302 (13), 272 (26), 197 (19), 183 (21), 169 (18), 115 (22), 103(11), 77 (12). Anal. Calcd for $C_{21}H_{18}ClNO_3$: C, 68.57; H, 4.93; N, 3.81. Found: C, 68.45; H, 4.85; N, 3.92%.

Preparation of 3-(3',4'-dimethoxyphenyl)-2,3,3a,4,5,10-hexahydropyrazolo[3,4-a]carbazoles (**3**): *general procedure*

The respective 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2a–e**, 0.001 mol) was dissolved in absolute ethanol (20 ml). Hydrazine hydrate (0.5 ml, 0.01 mol) was added to this mixture, which was then refluxed for 6 h, while the progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure. The crude mixture was poured into ice cold water and extracted with ethyl acetate, then washed with water and the combined organic layers dried over anhydrous sodium sulfate. Evaporation of the solvent followed by silica gel column chromatography using petroleum ether: ethyl acetate (95 : 5) as eluent yielded 2,3,3a,4,5,10-hexahydro-3-(3',4'-dimethoxyphenyl)pyrazolo[3,4-*a*]carbazole (**3a–e**). The product was recrystallised from ethanol.

3-(3',4'-Dimethoxyphenyl)-2,3,3a,4,5,10-hexahydro-7-methylpyrazolo [3,4-a]carbazole (**3a**): Yellow solid (0.270 g, 75%), m.p. 155–157 °C. IR: ν_{max} 3440, 1596, 1515, 1456, 1358, 1262, 805 cm^{-1}. ^1H NMR: δ 8.60 (b s, 1H, N_{10}–H), 7.31 (d, 1H, C_5'–H, J = 8.52 Hz), 7.29 (s, 1H, C_2'–H), 7.14(d, 1H, C_6'–H, J = 8.52 Hz), 6.77 (d, 1H, C_8 –H, J = 8.40 Hz), 6.61 (d, 1H, C_9–H, J = 8.40 Hz), 6.59 (s,1H, C_6–H), 5.66 (b s,1H, pyrazolo NH), 3.97 (s, 3H, C_3'–OCH_3), 3.95 (s, 3H, C_4'–OCH_3), 3.10 (m, 1H, C_3–H_2), 2.89 (m, 2H, C_5–H_2), 2.78 (m, 1H, C_{3a}–H), 2.52 (m, 2H, C_4–H_2), 2.47 (s, 3H, C_7-CH_3). MS: *m/z* (%) 361(M^+, 82), 346 (23), 224 (27), 218 (14), 197 (24), 168 (11), 143

(15), 107 (14), 91 (19).Anal. Calcd for $C_{22}H_{23}N_3O_2$: C, 73.11; H, 6.47; N, 11.63. Found: C, 73.09; H, 6.35; N, 11.52%.

3-(3',4'-Dimethoxyphenyl)-2,3,3a,4,5,10-hexahydro-8-methylpyrazolo[3,4-a]carbazole (**3b**): Pale yellow solid (0.249 g, 69%), m.p. 159–161 °C. IR: ν_{max} 3390, 1617, 1513, 1336, 1261, 806 cm^{-1}. ^{1}H NMR: δ 8.72 (b s, 1H, N_{10}–H), 7.74 (d, 1H, C_5'–H, *J* = 8.04 Hz), 7.51 (s, 1H, C_2'–H), 7.42 (d, 1H, C_6'–H, *J* = 8.04 Hz), 6.92 (d, 1H, C_6 –H, *J* = 7.08 Hz), 6.86 (d, 1H, C_7–H, *J* = 7.08 Hz), 6.82 (s,1H, C_9–H), 5.45 (b s, 1H, pyrazolo NH), 3.95 (s, 3H, C_3'–OCH_3), 3.92 (s, 3H, C_4'–OCH_3), 2.82 (m, 1H, C_3–H), 2.74 (m, 2H, C_5–H_2), 2.69 (m, 1H, C_{3a}–H), 2.65 (m, 2H, C_4–H_2), 2.47 (s, 3H, C_8-CH_3). MS: *m/z* (%) 361(M^+, 96), 346 (24), 218 (11), 195 (13), 197 (22), 168 (16), 115 (10), 103 (11). Anal. Calcd for $C_{22}H_{23}N_3O_2$: C, 73.11; H, 6.47; N, 11.63. Found: C, 73.04; H, 6.45; N, 11.71%.

3-(3',4'-Dimethoxyphenyl)-2,3,3a,4,5,10-hexahydro-9-methylpyrazolo[3,4-a]carbazole (**3c**): Pale yellow solid (0.252 g, 70%), m.p. 141–143 °C. IR: ν_{max} 3424, 1597, 1513, 1377, 1263, 1026 cm^{-1}. ^{1}H NMR: δ 8.89 (b s, 1H, N_{10}–H), 8.01 (s, 1H, C_2'–H), 7.76–6.89 (m, 5H, C_6,C_7, C_8, C_5', C_6'–H), 5.60 (b s, 1H, pyrazolo NH), 3.88 (s, 3H, C_3'–OCH_3), 3.85 (s, 3H, C_4'–OCH_3), 2.95–2.83 (m, 6H, C_3–H, C_{3a}–H, C_4–H_2, C_5–H_2), 2.52 (s, 3H, C_9–CH_3). MS: *m/z* (%) 361(M^+, 100), 346 (19), 312 (10), 276 (18), 210 (17), 195 (22), 114 (11), 107 (14), 91 (12). Anal. Calcd for $C_{22}H_{23}N_3O_2$: C, 73.11; H, 6.47; N, 11.63. Found: C, 73.21; H, 6.52; N, 11.54%.

3-(3',4'-Dimethoxyphenyl)-2,3,3a,4,5,10-hexahydropyrazolo[3,4-a]carbazole (**3d**): Pale yellow solid (0.236 g, 68%), m.p. 137–139 °C. IR: ν_{max} 3313, 1620, 1531, 1456, 1378, 1265, 1025, 806 cm^{-1}. ^{1}H NMR: δ 9.04 (b s, 1H, N_{10}–H), 8.82 (s, 1H, C_2'–H), 7.73–6.94 (m, 6H, C_6,C_7, C_8, C_9, C_5', C_6'–H), 5.72 (b s, 1H, pyrazolo NH), 3.89 (s, 3H, C_3'–OCH_3), 3.86 (s, 3H, C_4'–OCH_3), 2.95-2.63 (m, 6H, C_3–H, C_{3a}–H, C_4–H_2, C_5–H_2). MS: *m/z* (%) 347 (M^+, 100), 286 (16), 210 (20), 168 (14), 137 (24), 114 (18), 105 (11), 78 (17). Anal. Calcd for $C_{21}H_{21}N_3O_2$: C, 72.60; H, 6.09; N, 12.10. Found: C, 72.41; H, 6.05; N, 12.17%.

7-Chloro-3-(3',4'-dimethoxyphenyl)-2,3,3a,4,5,10-hexahydropyrazolo[3,4-a]carbazole (**3e**): Yellow solid (0.243 g, 64%), m.p. 143–145 °C. IR: ν_{max} 3414, 1617, 1513, 1454, 1379, 1025, 1144, 807 cm^{-1}. ^{1}H NMR: δ 8.98 (b s, 1H, N_{10}–H), 8.74 (s, 1H, C_2'–H), 7.94–6.89 (m, 5H, C_6, C_8, C_9, C_5', C_6'–H), 5.72 (b s, 1H, pyrazolo NH), 3.86 (s, 3H, C_3'–OCH_3), 3.84 (s, 3H, C_4'–OCH_3), 3.34-3.05 (m, 6H, C_3–H, C_{3a}–H, C_4–H_2, C_5–H_2), MS: *m/z* (%) 383/381 (M^+, 18/62), 346 (27), 319 (20), 210 (12), 195 (24), 114 (11), 91 (19). Anal. Calcd for $C_{21}H_{20}ClN_3O_2$: C, 66.05; H, 5.28; N, 11.00. Found: C, 65.91; H, 5.15; N, 11.11%.

Preparation of 3-(3',4'-dimethoxyphenyl)-4,5-dihydroisoxazolo[3,4-a]carbazoles (**4**): *general procedure*

The respective 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2a–e**, 0.001 mol) was treated with hydroxylamine hydrochloride (1 g, 0.014 mol) in pyridine (5 ml) at 130 °C for 8 h. After completion of the reaction, the crude mixture was poured into ice cold water and neutralised with 5N HCl, and the resulting semi-solid separated was extracted with chloroform. The combined organic layers were dried over anhydrous sodium sulfate. After the removal of solvent it was purified by silica gel column chromatography using petroleum ether : ethyl acetate (98 : 2) as eluent to yield 4,5-dihydro-3-(3',4'-dimethoxyphenyl)isoxazolo[3,4-*a*]carbazole (**4a–e**). The product thus obtained was recrystallised from ethanol.

3-(3',4'-Dimethoxyphenyl)-4,5-dihydro-7-methylisoxazolo[3,4-a]carbazole (**4a**): Pale yellow solid (0.252 g, 70%), m.p. 121–123 °C. IR: ν_{max} 3436, 1611, 1512, 1453, 1329, 1256, 1026, 789 cm^{-1}. ^{1}H NMR: δ 9.05 (b s, 1H, N_{10}–H), 7.52 (s, 1H, C_2'–H), 7.44–6.80 (m, 5H, C_6, C_8, C_9, C_5', C_6'–H), 3.86 (s, 3H, C_3'–OCH_3), 3.83 (s, 3H, C_4'–OCH_3), 3.15 (m, 2H, C_4–H_2), 2.97 (m, 2H, C_5–H_2), 2.52 (s, 3H, C_7-CH_3). MS: *m/z* (%) 360 (M^+, 100), 345 (19), 223 (19), 209 (18), 137 (20), 115 (16), 103 (18), 95 (11). Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.14; H, 5.45; N, 7.67%.

3-(3',4'-Dimethoxyphenyl)-4,5-dihydro-8-methylisoxazolo[3,4-a]carbazole (**4b**): Pale yellow solid (0.259 g, 72%), m.p. 132–135 °C. IR: ν_{max} 3400, 1604, 1509, 1457, 1357, 1246, 759 cm^{-1}. ^{1}H NMR: δ 9.13 (b s, 1H, N_{10}–H), 7.46–6.87 (m, 6H, C_6, C_7, C_9, C_2', C_5', C_6'–H), 3.91 (s, 3H, C_3'–OCH_3), 3.88 (s, 3H, C_4'–OCH_3), 3.22 (m, 2H, C_4–H_2), 2.92 (m, 2H, C_5–H_2), 2.47 (s, 3H, C_8–CH_3). MS: *m/z* (%) 360 (M^+, 86), 345 (27), 268 (11), 214 (19), 223 (16), 209 (11), 114 (22), 87 (16). Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.11; H, 5.44; N, 7.61%.

3-(3',4'-Dimethoxyphenyl)-4,5-dihydro-9-methylisoxazolo[3,4-a]carbazole (**4c**): Pale yellow solid (0.266 g, 74%), m.p. 180–182 °C. IR: ν_{max} 3426, 1614, 1512, 1456, 1380, 1260, 805 cm^{-1}. ^{1}H NMR: δ 10.26 (b s, 1H, N_{10}–H), 7.44-6.93 (m, 6H, C_6, C_7, C_8, C_2', C_5', C_6'–H), 3.78 (s, 3H, C_3'–OCH_3), 3.77 (s, 3H, C_4'–OCH_3), 3.02 (m, 2H, C_4–H_2), 2.78 (m, 2H, C_5–H_2), 2.50 (s, 3H, C_9–CH_3). MS: *m/z* (%) 360 (M^+,100), 345 (19), 307 (18), 268 (17), 237 (14), 211 (18), 114 (18), 103 (10). Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.17; H, 5.46; N, 7.61%.

3-(3',4'-Dimethoxyphenyl)-4,5-dihydroisoxazolo[3,4-a]carbazole (**4d**): Pale yellow solid (0.261 g, 75%), m.p. 194–196 °C. IR: ν_{max} 3431, 1601, 1515, 1456, 1358, 1142, 795 cm^{-1}. ^{1}H NMR: δ 9.85 (b s, 1H, N_{10}–H), 7.62–6.91 (m, 7H, C_6, C_7, C_8, C_9, C_2', C_5', C_6'–H), 3.83 (s, 3H, C_3'–OCH_3), 3.81 (s, 3H, C_4'–OCH_3), 2.95 (m, 2H, C_4–H_2), 2.19 (m, 2H, C_5–H_2). MS: *m/z* (%) 346 (M^+, 100), 315 (14), 301 (11), 284 (17), 167 (18), 119 (17), 115 (10), 76 (11), 43 (14). Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.97; H, 5.36; N, 8.21%.

7-Chloro-3-(3',4'-dimethoxyphenyl)-4,5-dihydroisoxazolo[3,4-a]carbazole (**4e**): Pale yellow solid (0.254 g, 67%), m.p. 119–121 °C. IR: ν_{max} 3423, 1609, 1514, 1455, 1358, 1262, 1024, 804 cm^{-1}. ^{1}H NMR: δ 9.86 (b s, 1H, N_{10}–H), 7.64-6.86 (m, 6H, C_6, C_8, C_9, C_2', C_5', C_6'–H), 3.91 (s, 3H, C_3'–OCH_3), 3.89 (s, 3H, C_4'–OCH_3), 3.08 (m, 2H, C_4–H_2), 2.91 (m, 2H, C_5–H_2). MS: *m/z* (%) 382/380 (M^+, 12/47), 351 (12), 345 (13), 243 (19), 209 (12), 195 (14), 167(15), 107 (20), 43 (12). Anal. Calcd for $C_{21}H_{17}ClN_2O_3$: C, 66.23; H, 4.50; N, 7.36. Found: C, 66.37; H, 4.56; N, 7.27%.

Preparation of 4-(3',4'-dimethoxyphenyl)-2-ethoxy-5,6-dihydropyrido[2,3-a]carbazole-3-carbonitriles (**5**): *general procedure*

A solution of the respective 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2a–e**, 1 mmol) in dry ethanol (20 ml) was added to an ice-cooled solution of sodium hydride (1.00 g, degreased with petroleum ether) in dry benzene (10 ml). To this mixture malononitrile (5 mmol) was added and the mixture was refluxed on a water bath for five hours. After the reaction was complete, the excess of solvent was removed by distillation and the mixture was poured into ice-water. The reaction mixture was then neutralised with ice-cold 6N HCl and extracted with ethyl acetate (3 × 50 ml). The organic layer was thoroughly washed with water and dried over anhydrous sodium sulfate. Upon removal of the solvent a brown crude mixture was obtained. It was purified by column chromatography over silica gel using petroleum ether: ethyl acetate (95 : 5) mixture as eluent to afford 4-(3',4'-dimethoxyphenyl)-2-ethoxy-5,6-dihydropyrido[2,3-*a*] carbazole-3-carbonitrile (**5**) as the product, which was recrystallised from ethanol to obtain yellow prisms.

4-(3',4'-Dimethoxyphenyl)-2-ethoxy-5,6-dihydro-8-methylpyrido[2,3-a]carbazole-3-carbonitrile (**5a**): Yellow prisms (0.325 g, 74%), m.p. 203–205 °C. IR: ν_{max} 3330, 2214, 1595, 1454, 1368, 1024, 804 cm^{-1}. ^{1}H NMR: δ 8.75 (b s, 1H, N_{11}–H), 7.44 (d, 1H, C_9–H, J_m = 1.97 Hz, J_o = 8.68 Hz), 7.35 (s, 1H, C_2'–H), 7.14 (d, 1H, C_6'–H, *J* = 7.20 Hz), 7.05 (d, 1H, C_{10}–H, *J* = 8.68 Hz), 6.95 (d, 1H, C_5'–H, *J* = 7.20 Hz), 6.87 (s, 1H, C_7–H), 4.64 (q, 2H, C_2–O$CH_2$$CH_3$, *J* = 7.04 Hz), 3.93 (s, 3H, C_3'–OCH_3), 3.89 (s, 3H, C_4'–OCH_3), 2.91-2.85 (m, 4H, C_5–H_2, C_6–H_2), 2.45 (s, 3H, C_8–CH_3), 1.52 (t, 3H, C_2–OCH_2CH_3, *J* = 7.04 Hz). MS: *m/z* (%) 439 (M^+,100), 424 (16), 302 (19), 288 (21), 277 (14), 233 (17), 219 (12), 181 (18), 167 (11), 114 (20). Anal. Calcd for $C_{27}H_{25}N_3O_3$: C, 73.78; H, 5.73; N, 9.56. Found: C, 73.67; H, 5.85; N, 9.60%.

4-(3',4'-Dimethoxyphenyl)-2-ethoxy-5,6-dihydro-9-methylpyrido[2,3-a]carbazole-3-carbonitrile (**5b**): Yellow solid (0.308 g, 70%), m.p. 106–108 °C. IR: ν_{max} 3328, 2217, 1588, 1355, 1213, 798 cm^{-1}. ^{1}H NMR: δ 8.64 (b s, 1H, N_{11}–H), 7.46 (d, 1H, C_7 –H, *J* = 7.76 Hz), 7.36 (s, 1H, C_2'–H), 7.15 (d, 1H, C_5'–H, *J* = 8.60 Hz), 7.01 (d, 1H, C_6'–H, *J* = 8.60 Hz), 6.99 (s, 1H, C_{10}–H), 6.85 (d, 1H, C_8–H, *J* = 7.76 Hz), 4.59 (q, 2H, C_2–O$CH_2$$CH_3$, *J* = 7.16 Hz), 3.93 (s, 3H, C_3'–OCH_3), 3.91 (s, 3H, C_4'–OCH_3), 2.93–2.88 (m, 4H, C_5–H_2, C_6–H_2), 2.49 (s, 3H, C_9-CH_3), 1.56 (t, 3H, C_2–OCH_2CH_3, *J* = 7.16 Hz). MS: *m/z* (%) 439 (M^+,100), 424 (22), 372 (14), 288 (12), 274 (14), 226 (18), 219 (18), 181 (12), 107 (10). Anal. Calcd for $C_{27}H_{25}N_3O_3$: C, 73.78; H, 5.73; N, 9.56. Found: C, 73.87; H, 5.81; N, 9.49%.

4-(3',4'-Dimethoxyphenyl)-2-ethoxy-5,6-dihydro-10-methylpyrido[2,3-a]carbazole-3-carbonitrile (**5c**): Yellow prisms (0.335 g, 76%), m.p. 109–111 °C. IR: ν_{max} 3430, 2218, 1596, 1358, 1258, 1022 cm^{-1}. ^{1}H NMR: δ 8.59 (b s, 1H, N_{11}–H), 7.33–7.26 (m, 3H, C_7, C_8, C_9–H), 7.06 (d, 1H, C_6'–H, *J* = 8.04 Hz), 6.93 (d, 1H, C_5'–H, *J* = 8.04 Hz), 6.85 (s, 1H, C_2'–H), 4.61 (q, 2H, C_2–O$CH_2$$CH_3$, *J* = 7.00 Hz), 3.95 (s, 3H, C_3'–OCH_3), 3.93 (s, 3H, C_4'–OCH_3), 2.96–2.89 (m, 4H, C_5–H_2, C_6–H_2), 2.58 (s, 3H, C_{10}–CH_3), 1.53 (t, 3H, C_2–OCH_2CH_3, *J* = 7.00 Hz). MS: *m/z* (%) 439 (M^+, 76), 380 (16), 355 (11), 288 (14), 212 (14), 195 (10), 181 (17), 114 (11). Anal. Calcd for $C_{27}H_{25}N_3O_3$: C, 73.78; H, 5.73; N, 9.56. Found: C, 73.48; H, 5.59; N, 9.42%.

4-(3',4'-Dimethoxyphenyl)-2-ethoxy-5,6-dihydropyrido[2,3-a] carbazole-3-carbonitrile (**5d**): Yellow solid (0.344 g, 81%), m.p. 212–213 °C. IR: ν_{max} 3382, 2214, 1597, 1336, 1253, 1025, 802 cm^{-1}. ^{1}H NMR: δ 8.77 (b s, 1H, N_{11}–H), 7.59–6.85 (m, 7H, C_7, C_8, C_9, C_{10}, C_2' C_5', C_6'–H), 4.63 (q, 2H, C_2–O*CH*$_2$CH$_3$, *J* = 7.20 Hz), 3.95 (s, 3H, C_3'–OCH$_3$), 3.92 (s, 3H, C_4'–OCH$_3$), 2.98–2.88 (m, 4H, C_5–H$_2$, C_6–H$_2$), 1.51 (t, 3H, C_2–OCH$_2$C*H*$_3$, *J* = 7.20 Hz).MS: *m/z* (%) 425 (M$^+$, 100), 394 (18), 369 (12), 325 (10), 219 (16), 197 (13), 195 (11), 137 (19), 115 (14), 43 (16). Anal. Calcd for $C_{26}H_{23}N_3O_3$: C, 73.79; H, 5.45; N, 9.88. Found: C, 73.48; H, 5.55; N, 9.75%.

8-Chloro-4-(3',4'-dimethoxyphenyl)-2-ethoxy-5,6-dihydropyrido [2,3-a]carbazole-3-carbonitrile (**5e**): Yellow solid (0.326 g, 71%), m.p. 179–181 °C. IR: ν_{max} 3381, 2217, 1567, 1348, 1253, 1043, 801 cm^{-1}. ^{1}H NMR: δ 8.25 (b s, 1H, N_{11}–H), 7.52–6.88 (m, 6H, C_7, C_9, C_{10}, C_2' C_5', C_6'–H), 4.62 (q, 2H, C_2–O*CH*$_2$CH$_3$, *J* = 7.00 Hz), 3.96 (s, 3H, C_3'–OCH$_3$), 3.92 (s, 3H, C_4'–OCH$_3$), 2.79–2.74 (m, 4H, C_5–H$_2$, C_6–H$_2$), 1.54 (t, 3H, C_2–OCH$_2$C*H*$_3$, *J* = 7.00 Hz). MS: *m/z* (%) 461/459 (M$^+$, 22/79), 424 (12), 394 (17), 369 (21), 325 (11), 269 (10), 219 (18), 137 (11), 114 (11). Anal. Calcd for $C_{26}H_{22}ClN_3O_3$: C, 67.90; H, 4.82; N, 9.14. Found: C, 67.68; H, 4.75; N, 9.32%.

Preparation of 2-amino-4-(3',4'-dimethoxyphenyl)pyrimido[4,5-a]-carbazoles (**6**): *general procedure.*

To 1.00 g of sodium hydride (degreased with petroleum ether) in dry benzene (10 ml), the respective 2-(3',4'-dimethoxybenzylidene)-2,3,4,9-tetrahydrocarbazol-1-one (**2a–e**, 1 mmol) and guanidine nitrate (10 mmol) were added and the mixture was refluxed for 18 h. The reaction was monitored by TLC. After completion of the reaction, the excess of solvent was boiled off and the residue was poured onto crushed ice. The reaction mixture was then neutralised and extracted with chloroform (3 × 40 ml). The organic layer was washed with water and dried over anhydrous sodium sulfate. Upon removal of the solvent a brown mass was obtained. It was purified by column chromatography over silica gel using petroleum ether : ethyl acetate (80 : 20) mixture as eluent to afford a yellow solid which was recrystallised from ethanol to yield the 2-amino-4-(3',4'-dimethoxyphenyl)pyrimido[4,5-*a*]carbazoles (**6a–e**).

2-Amino-4-(3',4'-dimethoxyphenyl)-8-methylpyrimido[4,5-a] carbazole (**6a**): Yellow solid (0.264 g, 69%), m.p. 218–220 °C. IR: ν_{max} 3443, 3189, 3157, 1607, 1534, 1379, 1257, 801 cm^{-1}. ^{1}H NMR: δ 9.55 (b s, 1H, N_{11}–H), 7.87(d, 1H, C_9–H, *J* = 8.72 Hz), 7.70 (d, 1H, C_{10}–H, *J* = 8.72 Hz), 7.45–7.26 (m, 6H, C_7, C_9, C_{10}, C_2', C_5', C_6'–H), 5.42 (b s, 2H, NH_2), 3.99 (s, 3H, C_3'–OCH$_3$), 3.95 (s, 3H, C_4'–OCH$_3$), 2.56 (s, 3H, C_8–CH$_3$). MS: *m/z* (%) 384 (M$^+$, 62), 369 (14), 360 (11), 354 (22), 298 (11), 218 (14), 195 (10), 165 (12), 114 (17). Anal. Calcd for $C_{23}H_{20}N_4O_2$: C, 71.86; H, 5.24; N, 14.57. Found: C, 71.79; H, 5.45; N, 14.32%.

2-Amino-4-(3',4'-dimethoxyphenyl)-9-methylpyrimido[4,5-a] carbazole (**6b**): Yellow solid (0.253 g, 69%), m.p. 222–225 °C. IR: ν_{max} 3374, 3204, 3194, 1598, 1380, 1259, 1027, 758 cm^{-1}. ^{1}H NMR: δ 8.98 (b s, 1H, N_{11}–H), 8.01–7.06 (m, 8H, C_5, C_6, C_7, C_8, C_{10}, C_2', C_5', C_6'–H), 5.56 (b s, 2H, NH_2), 3.91 (s, 3H, C_3'–OCH$_3$), 3.89 (s, 3H, C_4'–OCH$_3$), 2.58 (s, 3H, C_9–CH$_3$). MS: *m/z* (%) 384 (M$^+$, 100), 369 (22), 354 (19), 294 (18), 218 (11), 195 (16), 165 (14), 114 (11), 54 (15). Anal. Calcd for $C_{23}H_{20}N_4O_2$: C, 71.86; H, 5.24; N, 14.57. Found: C, 71.43; H, 5.35; N, 14.39%.

2-Amino-4-(3',4'-dimethoxyphenyl)-10-methylpyrimido[4,5-a]carbazole (**6c**): Yellow solid (0.276 g, 72%), m.p. 212–214 °C. IR: ν_{max} 3371, 3150, 3142, 1604, 1384, 1258, 807 cm^{-1}. ^{1}H NMR: δ 8.92 (b s, 1H, N_{11}–H), 7.98–7.25 (m, 8H, C_5, C_6, C_7, C_8, C_9, C_2', C_5', C_6'–H), 5.59 (b s, 2H, NH_2), 3.99 (s, 3H, C_3'–OCH$_3$), 3.96 (s, 3H, C_4'–OCH$_3$), 2.68 (s, 3H, C_{10}–CH$_3$). MS: *m/z* (%) 384 (M$^+$, 100), 376 (27), 369 (12), 276 (15), 233 (34), 197 (10), 195 (16), 114 (10). Anal. Calcd for $C_{23}H_{20}N_4O_2$: C, 71.86; H, 5.24; N, 14.57. Found: C, 71.95; H, 5.34; N, 14.49%.

2-Amino-4-(3',4'-dimethoxyphenyl)pyrimido[4,5-a]carbazole (**6d**): Yellow solid (0.240 g, 65%), m.p. 138–140 °C. IR: ν_{max} 3435, 3172, 3166, 1595, 1457, 1259, 754 cm^{-1}. ^{1}H NMR: δ 9.01 (b s, 1H, N_{11}–H), 7.88–7.20 (m, 9H, C_5, C_6, C_7, C_8, C_9, C_{10}, C_2', C_5', C_6'–H), 5.92 (b s, 2H, –NH_2), 3.96(s, 3H, C_3'–OCH$_3$), 3.94 (s, 3H, C_4'–OCH$_3$). MS: *m/z* (%) 370 (M$^+$, 100), 354 (26), 339 (16), 309 (21), 233 (11), 218 (18), 195 (12), 176 (14), 115 (19), 104 (17), 79 (10). Anal. Calcd for $C_{22}H_{18}N_4O_2$: C, 71.34; H, 4.90; N, 15.13. Found: C, 71.55; H, 5.01; N, 14.98%.

2-Amino-8-chloro-4-(3',4'-dimethoxyphenyl)pyrimido[4,5-a] carbazole (**6e**): Yellow solid (0.251 g, 62%), m.p. 189–191 °C. IR: ν_{max} 3439, 3186, 3182, 1593, 1459, 1383, 1043, 804 cm^{-1}. ^{1}H NMR: δ 9.11 (b s, 1H, N_{11}–H), 7.80–7.22 (m, 8H, C_5, C_6, C_7, C_9, C_{10}, C_2', C_5', C_6'–H), 5.89 (b s, 2H, NH_2), 3.88(s, 3H, C_3'–OCH$_3$), 3.86 (s, 3H, C_4'–OCH$_3$). MS: *m/z* (%) 406/404 (M$^+$, 16/54), 354 (16), 324 (37), 369 (22), 294 (11), 233 (20), 187 (14), 156 (16), 114(18). Anal. Calcd for $C_{22}H_{17}ClN_4O_2$: C, 65.27; H, 4.23; N, 13.86. Found: C, 65.55; H, 4.39; N, 13.49%.

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