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Synthesis of some pyrazino, pyrimido and mercaptopyrimido annelated carbazoles using 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazoles

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Treatment of 1-oxo-2-hydroxymethylene-1,2,3,4-tetrahydrocarbazole **1** with hydrazine hydrate, hydroxylamine hydrochloride, urea and thiourea in the presence of gl. acetic acid afforded the novel carbazole derivatives namely 4,5-dihydro-2*H*-pyrazino [3,4-*a*]carbazoles **2**, 2-cyano-1-hydroxycarbazoles **3**, 2,4-dihydroxy-1,4,5,6-tetrahydro-pyrimido[4,5-*a*]carbazoles **4** and 4-hydroxy-2-mercapto-1,4,5,6-tetrahydropyrimido- [4,5-*a*]carbazoles **5** respectively.

Keywords: 1-oxo-2-hydroxymethylene-1,2,3,4-tetrahydrocarbazole, 4,5-dihydro-2*H*-pyrazino[3,4-*a*]carbazoles, 2-cyano-1-hydroxycarbazoles, 2,4-dihydroxy-1,4,5,6-tetra-hydropyrimido[4,5-*a*]carbazoles, 4-hydroxy-2-mercapto-1,4,5,6-tetrahydro-pyrimido- [4,5-*a*]carbazoles

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Among the nitrogenous plant constituents carbazole derivatives, a special class of indole alkaloids have attracted considerable attention owing to their diverse physiological activities[1,2]. These compounds are considered to represent potential therapeutic agents against a variety of diseases initiated by oxygen derived free radicals like myocardial, arteriosclerosis, inflammation, rheumatism, senility, cancer and autoimmune diseases[3-5]. Although a large number of reports are available in literature describing the synthetic methods directed towards ellipticine, olivacine and related tetracyclic compounds, the replacement of the pyridine ring in the natural structure by other heteroaromatic systems has been reported[6-9]. In particular heterocyclo-fused dihydro- and tetrahydrocarbazoles have been associated with interesting various pharmacological as well as biological properties[6-9]. For example, pyrazino[3,2,1-*j*,*k*]carbazoles exhibited psychotropic and antidepressant properties. 1-Oxo-1,2,3,4-tetrahydrocarbazoles have demonstrated antihistamine and antiseratonin activities. 1-Carbomethoxy-1,2,3,4-tetrahydrocarbazoles and 1-hydroxymethylene-1,2,3,4-tetrahydrocarbazoles were found to have antiinflammatory and bacterial growth inhibitory properties respectively. 1-*N*,*N*-Dimethylamino-1,2,3,4-tetrahydrocarbozole acts as a CNS depressant agent[10-13]. But the synthetic methods reported for all aforementioned systems suffer from some limitations such as low yields. In this laboratory Prasad *et al*.[12-14] have attempted the synthesis of dihydro- and tetrahydro- carbazole alkaloids. We now present a full account of the synthesis of a number of pyrazino, isoxazolo, hydroxypyrimido and mercaptopyrimido annelated carbazole derivatives and their structural elucidation. In order to realize our target compounds, we used 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazoles **1** as suitable precursors, which have been prepared according to earlier reported procedure[15].

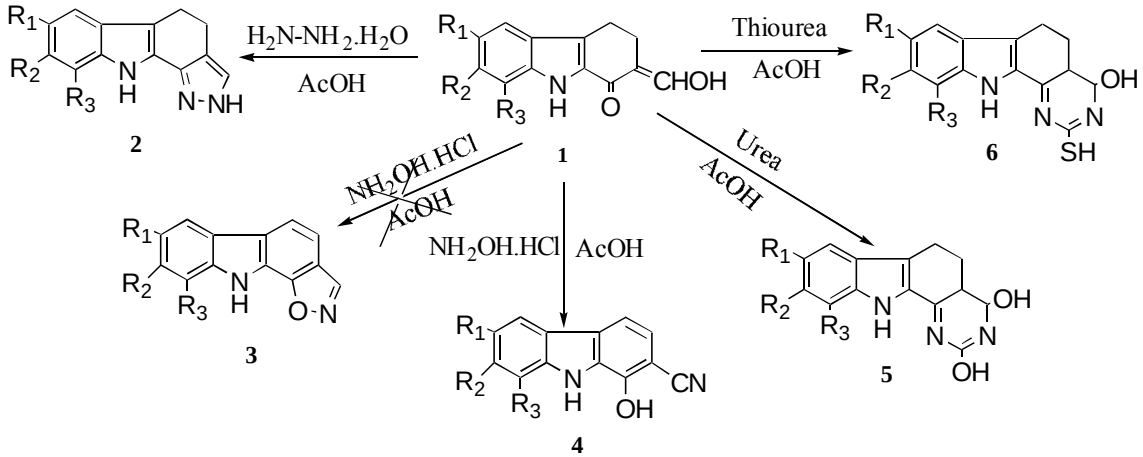
When 2-hydroxymethylene-6-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole (ref.15) **2a** was treated with hydrazine hydrate in acetic acid, it afforded the expected 7-methyl-4,5-dihydro-2*H*-pyrazino[3,4-*a*]-carbazole **2a** in 90% yield. Its IR spectrum revealed the presence of >C=N group and absence of carbonyl absorption. The ^{1}H NMR spectrum of **2a** showed a multiplet in the δ 2.89-2.91 region corresponding to C_4-H_2 and C_5-H_2 respectively along with a singlet at δ 12.45 for pyrazino-NH proton. C_8-H appeared as a doublet of doublet at δ 6.87 with J_{ortho} = 8.16 Hz and J_{meta} = 1.40 Hz, and a multiplet at δ 7.21-7.23 corresponding to C_6-H and C_9-H. The signal due to carbazole NH appeared as a broad singlet at δ 11.25.

The C_3-H proton appeared as a singlet at δ 7.52. The molecular ion peak in its mass spectrum at *m/z* 223 and the elemental analysis agreed well with the molecular formula $C_{14}H_{13}N_3$. On the basis of the spectral data and elemental analysis, the structure of **2a** was interpreted as 7-methyl-4,5-dihydro-2*H*-pyrazino[3,4-*a*]carbazole **2a**. Similar reactions were conducted with **1b**, **1c** and **1d** which yielded the corresponding pyrazino[3,4-*a*]carbazoles **2b**, **2c** and **2d** (**Scheme I**).

In another reaction, 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazole **1a** was treated with hydroxylamine hydrochloride in gl. acetic acid with an expectation to obtain the product **3a** as in the previous case. The reaction product after work-up showed the presence of a single product on TLC, which was purified by column chromatography. The IR spectrum of the compound registered two absorptions at 3425 and 3238 cm^{-1} which are ascribable for -OH and -NH stretching vibrations respectively. The ^1H NMR spectrum of the product exhibited the following resonances. A singlet for three protons at δ 2.47 and four number of one proton doublets at 7.26 (J_{ortho}= 8.20 Hz), 7.31 (J_{ortho}= 8.20 Hz), 7.52 (J_{ortho}= 8.10 Hz) and 7.72 (J_{ortho}= 8.10 Hz) respectively. Further, two singlets at δ 7.94 and 11.01 with integration for one proton and another broad singlet at δ 10.82 were also present. The presence of a singlet at δ 11.01 indicated that the expected product was not formed in this reaction. Further the presence of four doublets in the aromatic region was assigned for C_3, C_4, C_7 and C_8 protons. The two singlets appeared at δ 7.94 and 11.01 were assigned to C_5-H and OH protons respectively. A broad singlet at δ 10.82 was due to carbazole NH. The molecular ion peak in its mass spectrum at *m/z* 222 and the elemental analysis agreed well with the molecular formula $C_{14}H_{10}N_2O$. Based on the above mentioned spectral data the structure of product was assigned to be 2-cyano-6-methyl-1-hydroxycarbazole **4a**. Extension of the above reaction on **1b-d** afforded the corresponding 2-cyano-1-hydroxycarbazoles (**4b-d**, **Scheme I**).

A plausible mechanism for the conversion of 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazole **1** to 2-cyano-1-hydroxycarbazole **4** is depicted (**Scheme II**). As expected, hydroxylamine hydrochloride reacted with the more reactive C_2-formyl group to yield the intermediate **a** which subsequently loses a molecule of water to afford the nitrile intermediate **b**. Tautomerisation of the resulting 2-cyano-1-oxo-1,2,3,4-tetrahydrocarbazole intermediate **b** gives the enolic form **c**, which further under went aromatisation to give the final product **4**.

2-Hydroxymethylene-6-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole **1a** was treated with urea in gl. acetic acid for 5 hr and the reaction mixture after work-up gave a single product, which was characterized as 2,4-



1-6 **a**: $R_1 = CH_3$, $R_2 = R_3 = H$
b: $R_1 = R_3 = H$, $R_2 = CH_3$
c: $R_1 = R_2 = H$, $R_3 = CH_3$
d: $R_1 = R_2 = R_3 = H$

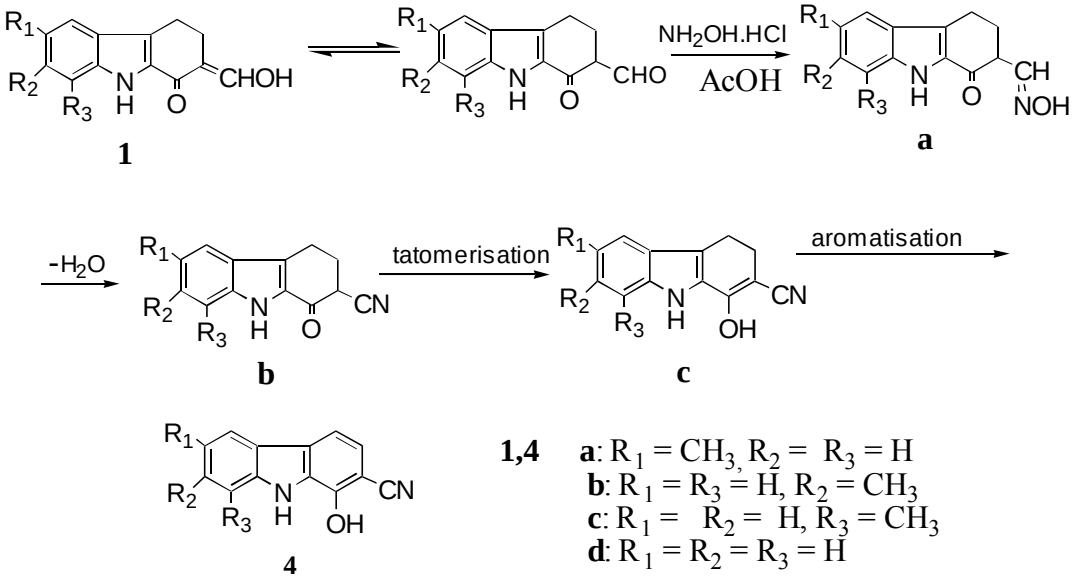
Scheme I

dihydroxy-8-methyl-1 ,4, 5,6-tetrahydropyrimido[4,5-*a*]carbazole **5a**. The IR spectrum of this compound showed strong absorption bands at 3306 and 3152 cm^{-1} for -OH and -NH groups respectively. The ^1H NMR spectrum of **5a** showed two multiplets at δ 2.74-2.77 and 2.89-2.90 for C_5-H_2 and C_6-H_2 protons and a singlet at 2.39 corresponding to three protons of C_8-CH_3 group. A broad singlet with two proton integration appeared at δ 6.88 is assigned to C_4-OH and C_2-OH. A doublet appeared at δ 7.31 with J_{ortho} = 8.08 Hz is assigned to C_9-H proton. An aromatic cluster with two proton integration appeared as a multiplet at δ 7.32-7.35 due to C_7-H and C_{10}-H and a singlet appeared at δ 7.42 for C_4-H proton. The resonance for N_{11}-H and N_1-H protons appeared as two broad singlets δ 10.48 and 11.36. The molecular ion peak in its mass spectrum at *m/z* 269 and the elemental analysis agreed well with the molecular formula $C_{15}H_{15}N_3O_2$.The generality of the above reaction was studied with **1b-d** and the corresponding 2,4-dihydroxy-1,4,5,6-tetrahydropyrimido[4,5-*a*]carbazoles **5b-d** were obtained (**Scheme I**).

Finally, 2-hydroxymethylene-6-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole **1a** was treated with thiourea in gl. acetic acid for 5 hr. This reaction yielded a single product which was found to be 4-hydroxy-2-mercapto-8-methyl-1,4,5,6-tetrahydropyrimido[4,5-*a*]carbazole **6a**. The IR spectrum of this compound exhibited three strong absorptions at 3197, 1541 and 1159 cm^{-1} indicating the presence of -NH group -CS-group and -SH group. The presence of sulphur was further confirmed by sodium nitroprusside positive test. Its ^1H NMR spectrum displayed a singlet for three protons at δ 2.39 assigned C_8-CH_3. Also, a multiplet for two protons in the region δ 2.78-2.80 assigned to C_5-H_2 protons and a multiplet for three protons in the region δ 2.39-3.03 due to C_6-H_2 and SH protons. A singlet appeared at δ 7.44 for C_7 proton and two doublets registered at δ 7.13 and 7.34 with J_{ortho} = 8.00 Hz for C_9 and C_{10} protons respectively and a singlet appeared at δ 7.84 was due to C_4-H proton. The presence of two broad singlets at δ 8.53 (N_{11}-H or N_1-H) and 8.59 (N_1-H or N_{11}-H) for two protons respectively and a singlet appeared at δ 11.46 was due to OH proton. These spectroscopic features in combination with the analytical data proved the structure of compound **6a** to be 4-hydroxy-2-mercapto-8-methyl-1,4,5,6-tetrahydropyrimido-[4,5-*a*]carbazole. The molecular ion peak in its mass spectrum appeared at *m/z* 285 and the elemental analysis agreed well with the molecular formula $C_{15}H_{15}N_3SO$. A series of similar compounds **6b-d** have been obtained from **1b-d** on reaction with thiourea in a similar manner as described for **6a** (**Scheme I**).

Experimental Section

Melting points were determined by Mettler FP-5 apparatus and are uncorrected. The reactions were monitored by TLC. Column chromatographic separations were done using silica gel 120 mesh (Silica gel for TLC with calcium sulphate binder). IR spectra were recorded on a Perkin-Elmer model 1600 FT-IR instrument as KBr pellets (**Table I**). ^1H NMR spectra (400 MHz) were recorded on a Varian AMX 400 spectrometer using TMS



Scheme II

Table I—Physical and IR spectral data of compounds **2a-d**, **4a-d**, **5a-d** and **6a-d**

Compd	m.p. °C	Yield (%)	IR cm^{-1}	Mol.Formula Mol. wt	Calcd (%) Found C	H	N
2a	215	90	3396,3261, 1590	$C_{14}H_{13}N_3$ (223.137)	(75.29 75.20	5.87 5.80	18.83) 18.80
2b	125	84	3310,3261, 1560	$C_{14}H_{13}N_3$ (223.137)	(75.29 75.28	5.87 5.89	18.83) 18.89
2c	100	85	3470,3180, 1570	$C_{14}H_{13}N_3$ (223.137)	(75.29 75.24	5.87 5.79	18.83) 18.84
2d	140	91	3470,3180, 1565	$C_{13}H_{11}N_3$ (209.120)	(74.60 74.65	5.30 5.38	20.09) 20.14
4a	220	80	3425,3238	$C_{14}H_{10}N_2O$ (222.106)	(75.64 75.60	04.53 04.50	12.61) 12.53
4b	215	80	3421,3246	$C_{14}H_{10}N_2O$ (222.106)	(75.64 75.65	04.53 04.55	12.61) 12.50
4c	230	82	3421,3220	$C_{14}H_{10}N_2O$ (222.106)	(75.64 75.69	04.53 04.59	12.61) 12.57
4d	225	79	3425,3238	$C_{13}H_8N_2O$ (208.219)	(74.98 74.96	03.87 03.81	13.45) 13.40
5a	232	65	3306,3152, 1581	$C_{15}H_{15}N_3O_2$ (269.202)	(66.90 66.94	5.61 5.65	15.60) 15.66
5b	215	55	3303,3165, 1556	$C_{15}H_{15}N_3O_2$ (269.202)	(66.90 66.91	5.61 5.66	15.60) 15.61
5c	240	68	3320,3282, 1571	$C_{15}H_{15}N_3O_2$ (269.202)	(66.90 66.95	5.61 5.67	15.60) 15.69
5d	225	64	3298,3168, 1556	$C_{14}H_{13}N_3O_2$ (255.257)	(65.87 65.81	05.13 05.10	16.87) 16.83
6a	220	80	3197,1159, 1541	$C_{15}H_{15}N_3SO$ (285.369)	(63.13 63.11	05.29 05.21	14.72) 14.70
6b	205	82	3178,1211, 1569	$C_{15}H_{15}N_3SO$ (285.369)	(63.13 63.15	05.29 05.20	14.72) 14.71
6c	236	85	3176,1152, 1541	$C_{15}H_{15}N_3SO$ (285.369)	(63.13 63.10	05.29 05.28	14.72) 14.79
6d	246	79	3195,1203, 1571	$C_{14}H_{13}N_3SO$ (271.342)	(61.97 61.95	04.82 04.80	15.48) 15.40

as an internal standard (**Table II**). Signal multiplicities are given as s (singlet), bs (broad singlet), d (doublet), dd (doublet of doublet) and m (multiplet). Electron impact (EI) mass spectra were recorded on a Jeol (D)-300 EI mass spectrometer.

Preparation of 4,5-dihydro-2*H*-pyrazino[3,4-*a*]carbazoles 2. A mixture of an appropriate 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazole (**1**, 1 mmole) and hydrazine hydrate (0.050 g, 1 mmole) was refluxed in gl. acetic acid (5 mL) at 120°C for 5 hr. The reaction mixture was then poured into crushed ice with stirring, the solid thus separated was filtered, dried and purified by column chromatographic technique using petroleum ether-ethyl acetate as a solvent system over silica gel which gave yellow crystals.

Preparation of 2-cyano-1-hydroxycarbazoles 4. The reaction mixture consisting of the appropriate 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazole (**1**, 1 mmole), hydroxylamine hydrochloride (0.069 g, 2 mmole) and gl. acetic acid (5 mL) was refluxed at 120°C for 5 hr. The reaction mixture was then poured into crushed ice with stirring, the precipitated crude product was filtered, washed, dried and purified by column chromatography over silica gel (eluting with petroleum ether-ethyl acetate, 90:10) to give the pure compound as white crystals.

Preparation of 2,4-dihydroxy-1,4,5,6-tetrahydro-pyrimido[4,5-*a*]carbazoles 5. A mixture of the respective 2-hydroxymethylene-1-oxo-1,2,3,4-tetra-hydrocarbazole (**1**, 1 mmole) and urea (0.060 g, 2 mmole) in gl. acetic acid (5 mL) was refluxed at 120°C for 5 hr. The reaction mixture was cooled and

Table II—NMR spectral data of compounds **2a-d**, **4a-d**, **5a-d** and **6a-d**

Compd	^{1}H NMR (δ, ppm)
2a	2.37 (s, 3H, C_7-CH_3), 2.89-2.91 (m, 4H, C_4-H_2 and C_5-H_2), 6.87 (dd, 1H, C_8-H, J_{ortho}= 8.16 Hz, J_{meta}= 1.4 Hz), 7.21-7.23 (m, 2H, C_6-H and C_9-H), 7.52 (s, 1H, C_3-H), 11.25 (bs,1H, carbazole-NH), 12.45 (bs, 1H, pyrazolino-NH).
2b	2.61 (s, 3H, C_8-CH_3), 2.83-2.86 (m, 2H, C_4-H_2), 3.17-3.20 (m, 2H, C_5-H_2), 6.70 (d, 1H, C_7-H, J_{ortho}= 8.88 Hz,), 7.18 (d, 1H, C_6-H, J_{ortho}= 8.08 Hz), 7.47-7.50 (m, 1H, C_9-H and 1H, C_3-H), 11.34 (bs, 1H, carbazole-NH), 12.48 (bs, 1H, pyrazolino-NH).
2c	2.65 (s, 3H, C_9-CH_3), 2.81-2.83 (m, 2H, C_4-H_2), 2.88-2.91 (m, 2H, C_5-H_2), 6.84 (d, 1H, C_8-H, J_{ortho}= 7 Hz), 6.89 (m, 1H, C_7-H), 7.28 (d, 1H, C_6-H, J_{ortho}= 7.6 Hz), 7.54 (s, 1H, C_3-H), 11.29 (bs, 1H, carbazole-NH), 12.51 (bs, 1H, pyrazolino-NH).
2d	2.81-2.85 (m, 2H, C_4-H_2), 2.91-2.93 (m, 2H, C_5-H_2), 7.21 (m, 1H, C_8-H), 7.38 (m, 1H, C_7-H), 7.49 (d, 1H, C_9-H, J_{ortho}= 8.48 Hz), 7.70 (d, 1H, C_6-H, J_{ortho}= 8.08 Hz), 8.19 (s, 1H, C_3-H), 11.27 (bs, 1H, carbazole-NH), 12.95 (bs, 1H, pyrazolino-NH).
4a	2.47 (s, 3H, C_6-CH_3), 7.26 (d, 1H, C_3-H, J_{ortho}= 8.20 Hz), 7.31 (d, 1H, C_4-H, J_{ortho}= 8.20 Hz), 7.52 (d, 1H, C_7-H, J_{ortho}= 8.10 Hz), 7.72 (d, 1H, C_8-H, J_{ortho}= 8.10 Hz), 7.94 (s, 1H, C_5-H), 10.82 (bs, 1H, NH), 11.01 (s, 1H, OH).
4b	2.49 (s, 3H, C_7-CH_3), 7.26 (d, 1H, C_3-H, J_{ortho}= 8.16 Hz), 7.31 (d, 1H, C_6-H, J_{ortho}= 8.24 Hz), 7.35 (s, 1H, C_8-H,), 7.70 (d, 1H, C_4-H, J_{ortho}= 8.16 Hz), 7.76 (d, 1H, C_5-H, J_{ortho}= 8.24 Hz), 10.84 (bs, 1H, NH), 11.25 (s, 1H, OH).
4c	2.58 (s, 3H, C_8-CH_3), 7.13-7.17 (m, 1H, C_6-H), 7.29-7.31 (m, 2H, C_3-H and C_4-H), 7.74 (d, 1H, C_7-H, J_{ortho}= 8.42 Hz), 7.99 (d, 1H, C_5-H, J_{ortho}= 8.42 Hz), 10.77 (bs, 1H, NH), 11.76 (s, 1H, OH).
4d	7.23 (m, 1H, C_7-H), 7.30 (d, 1H, C_3-H, J_{ortho}= 8.16 Hz), 7.48 (m, 1H, C_6-H,), 7.62 (d, 1H, C_4-H, J_{ortho}= 8.16 Hz), 7.77 (d, 1H, C_8-H, J_{ortho}= 8.16 Hz), 8.16 (d, 1H, C_5-H, J_{ortho}= 8.16 Hz), 10.89 (bs, 1H, NH), 11.16 (s, 1H, OH).
5a	2.39 (s, 3H, C_8-CH_3), 2.74-2.77 (m, 2H, C_5-H_2), 2.89-2.90 (m, 2H, C_6-H_2), 6.88 (b s, 2H, C_2-OH and C_4-OH), 7.31-7.35 (m, 3H, C_7-H, C_9-H and C_{10}-H), 7.42 (s, 1H, C_4-H) 10.48 (bs, 1H, N_{11}-H), 11.36 (bs, 1H, N_1-H).
5b	2.62 (s, 3H, C_9-CH_3), 2.75-2.79 (m, 2H, C_5-H_2), 3.17-3.19 (m, 2H, C_6-H_2), 6.78-6.79 (m, 6H, C_4-H, C_7-H, C_8-H, C_{10}-H, C_4-OH and C_2-OH), 10.47(bs, 1H, N_{11}-H), 11.44 (bs, 1H, N_1-H).
5c	2.52 (s, 3H, C_{10}-CH_3), 2.76-2.78 (m, 2H, C_5-H_2), 2.90-2.92 (m, 2H, C_6-H_2), 6.98(bs, 2H, C_4-OH and C_2-OH), 7.01-7.49 (m, 4H, C_4-H, C_7-H, C_8-H and C_9-H), 10.45 (bs,1H, N_{11}-H), 11.40 (bs, 1H, N_1-H).
5d	2.76-2.79 (m, 2H, C_5-H_2), 2.92-2.95 (m, 2H, C_6-H_2), 6.88 (bs, 2H, C_4-OH and C_2-OH), 7.06-7.67 (m, 5H, C_4-H, C_7-H, C_8-H, C_9-H and C_{10}-H), 10.48 (bs,1H, N_{11}-H), 11.49 (bs, 1H, N_1-H).
6a	2.39 (s, 3H, C_8-CH_3), 2.78-2.80 (m, 2H, C_5-H_2), 2.93-3.03 (m, 3H, C_6-H_2 and C_2-SH), 7.13 (d, 1H, C_9-H, J_{ortho}= 8.00 Hz), 7.34 (d, 1H, C_{10}-H J_{ortho} = 8.00 Hz), 7.44 (s, 1H, C_7-H), 7.84 (s, 1H, C_4-H), 8.53 (bs, 1H, N_{11}-H or N_1-H), 8.69 (m, 1H, N_1-H or N_{11}-H), 11.46 (bs, 1H, C_4-OH).
6b	2.41 (s, 3H, C_9-CH_3), 2.77-2.81 (m, 2H, C_5-H_2), 2.93-3.02 (m, 3H, C_6-H_2 and C_2-SH), 6.91 (d, 1H, C_8-H, J_{ortho}= 8.32 Hz), 7.29 (s, 1H, C_{10}-H), 7.56 (d, 1H, C_7-H, J_{ortho}= 8.32 Hz), 7.56 (s, 1H, C_4-H), 8.56 (bs, 1H, N_{11}-H or N_1-H), 8.71 (bs, 1H, N_1-H or N_{11}-H), 11.45 (bs, 1H, C_4-OH).
6c	2.51 (s, 3H, C_{10}-CH_3), 2.79-2.85 (m, 2H, C_5-H_2), 2.95-2.97 (m, 3H, C_6-H_2 and C_2-SH), 6.99-7.51 (m, 3H, C_7-H, C_8-H and C_9-H), 7.83 (s, 1H, C_4-H), 8.57 (bs, 1H, N_{11}-H or N_1-H), 8.70 (bs, 1H, N_1-H or N_{11}-H), 11.47 (bs, 1H, C_4-OH).
6d	2.80-2.84 (m, 2H, C_5-H_2), 2.96-3.05 (m, 3H, C_6-H_2 and C_2-SH), 7.05-7.69 (m, 5H, C_4-H, C_7-H, C_8-H, C_9-H and C_{10}-H), 8.59 (bs, 1H, N_{11}-H or N_1-H), 8.73 (bs, 1H, N_1-H or N_{11}-H), 11.47 (bs, 1H, C_4-OH).

poured into crushed ice, the solid thus separated out was filtered, washed with water, dried and purified by column chromatography over silica gel (eluting with petroleum ether-ethyl acetate, 75:25) to give yellow crystals.

Preparation of 4-hydroxy-2-mercapto-1,4,5,6-tetrahydropyrimido[4,5-*a*]carbazoles 6. The respective 2-hydroxymethylene-1-oxo-1,2,3,4-tetrahydrocarbazole (**1**, 1 mmole) and thiourea (0.076 g, 2 mmole) were dissolved in gl. acetic acid (5 mL) and the resulting solution was refluxed at 120°C for 5 hr. The reaction mixture was then cooled and poured into ice with stirring. The solid thus separated out was filtered, washed with water, dried and purified by column chromatographic technique using petroleum ether-ethyl acetate (75:25) as a solvent system over silica gel to give the pure compound orange coloured needles.

References

1 Lescot E, Muzard G, Markovits J, Belleney J, Roques B P & Le L B Pecq, *J Med Chem*, **1986**, 1731 and references cited therin.

2 Asselin A A, *J Med Chem*, 19, **1976**, 787.

3 Hammond B, Kantos H A & Hess M L, *Can J Physiol Pharmacol*, 63, **1985**, 173.

4 Cerutti P A, *Science*, 227, **1985**, 375.

5 Halliwell B & Gutteridge J M C, *Methods Enzymol*, 1, **1990**, 186.

6 Agarwal, Agarwall S K & Bhakuni D S, *Indian J Chem,* 31B, **1992**, 44.

7 Mahboobi S, Kuhr S & Koller M, *Tetrahedron*, 52, **1996**, 6373.

8 Peixoto F M C, Queiroz M J R P & Kirsch G, *J Chem Res* (M), 180, **1998**, 801.
9 Chunchatprasert L & Shannon P V R, *J Chem Soc Perkin Trans 1*, **1994**, 1765.
10 Sekar M, Vanitha C & Rajendra Prasad K J, *Z Naturforsch*, 49b, **1994**, 687.
11 Rajendra Prasad K J, Vijayalakshmi C S & Sowmithran D, *Org Prep Proced Int*, 27, **1995**, 686.
12 Sekar M & Rajendra Prasad K J, *Z Naturforsch*, 50b, **1995**, 687.
13 Shanmugasundaram K & Rajendra Prasad K J, *Z Naturforsch*, 54b, **1999**, 1202.
14 Sangeetha V & Rajendra Prasad K J, *Indian J Chem*, communicated.
15 Sangeetha V & Rajendra Prasad, *Heterocycles*, communicated.